SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 93 DECEMBER, 1951 NUMBER 6

ARTERIES, VEINS, AND ARTERIOVENOUS ANASTOMOSES IN THE HUMAN STOMACH

T. E. BARLOW, M.D., F. H. BENTLEY, M.D., F.R.C.S., and D. N. WALDER, M.D.,
Newcastle upon Tyne, England

IT is evident that in some tissues abnormal variations in blood flow can lead to disease processes. The variations are fleeting and physiologic in nature, and are not accompanied by any demonstrable organic disease of the vessel wall. They may occur, for instance, in response to unusual stresses in the mechanisms for maintaining blood pressure, or from the effects of injury, or from emotional disturbance. Such processes may be recognized in several organs, including the liver, central nervous system, or kidney.

Study of variations in blood flow through the vessels of the stomach in normal and abnormal states, though a difficult project, might well be rewarding. It is obviously impracticable however to study the gastric circulation without an understanding of the architecture of the pathways through which the blood flows. The available accounts of the vascular anatomy within the stomach wall are incomplete and, in some instances, contradictory. It seemed necessary therefore to study in detail the anatomy and distribution of the gastric arteries and veins within the different parts of the stomach. A first survey was begun in fortunate collaboration with the late Dr. A. E. Barclay of the Nuffield Institute for Medical Research, Oxford (3, 4), and has been continued in the laboratories in the Medical School, Newcastle upon Tyne.

Textbooks of anatomy indicate only briefly the minute distribution of the blood vessels in the stomach wall, but various accounts exist in the literature, of which the first of importance was that of Arnold (1847) who described and illustrated the vessels within the gastric mucosa. Disse (1904) defined and measured the branches in the submucosa and mucous membrane. His dissections led him to consider the mucosal arteries to be end-arteries.

A valuable study was made by Reeves (1920) which confirmed and expanded the work of Disse. Reeves emphasized that in the region of the lesser curve the arterial branches in the submucosa are more slender, and the anastomoses between adjacent branches are finer in caliber and fewer in number than in the anterior and posterior walls. Similar conclusions were reached by Jatrou (1920). Hoffman and Nather (1921) distinguished three areas of arterial supply, depending on the caliber of the anastomosing vessels and the manner in which the anastomoses are formed.

The most extensive and painstaking work was that of Djørup (1922) who described the results of dissection of 23 stomachs in which the vessels had been injected. He claimed that the mucosal arteries were not end-

From the Departments of Anatomy and of Surgery, King's College, Newcastle upon Tyne, in the University of Durham, England.

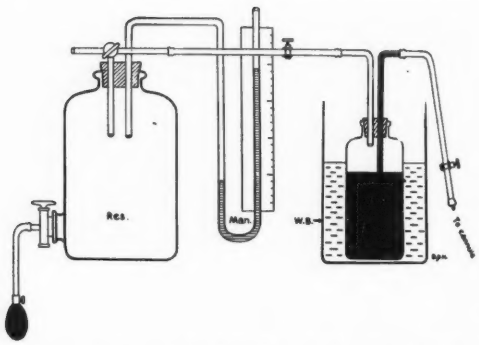

Fig. 1. Apparatus for injection of the vessels of the stomach.

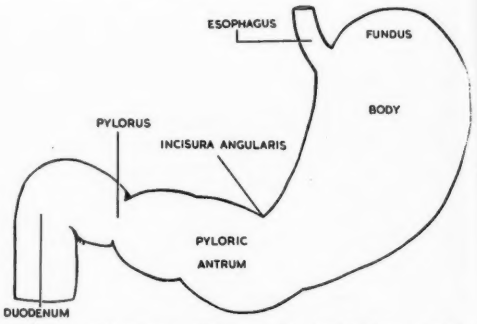

Fig. 2. Diagram to illustrate the terminology used in describing the different parts of the stomach.

arteries, but anastomosed on either side of the muscularis mucosae. The venous system was not considered. These different accounts are summarized by Babkin (1944).

Methods

Human stomachs removed post mortem from bodies without gastrointestinal disease were used for the first survey. When the general pattern of vessels had been determined, the investigation was continued in a more detailed manner on specimens taken from young and middle-aged males at operation for duodenal ulcer. The specimens consisted of the distal two-thirds of the stomach, together with the intact vascular chains on the greater and lesser curvatures, and were carried in Ringer solution at 37 degrees C. directly from the operating theater to the laboratory, where the vessels were injected within a few minutes of removal of the specimen from the body.

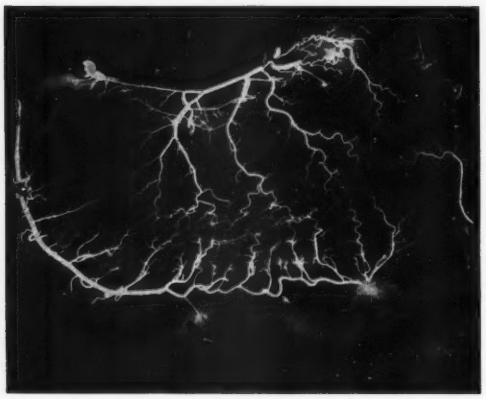

Fig. 3. Roentgenogram of the whole anterior wall of the stomach, showing the vascular chains on the greater and lesser curvatures and the plexus of vessels in the submucosa. Arteries filled with 20 per cent chlorbismol. ×0.27.

Injection techniques

Microradiology. Following the techniques described by Barclay (1947), a cannula was tied into the gastroepiploic artery, and another into the vein, on the greater curve of the stomach; in the case of operation specimens leakage was controlled from the cut ends of the stomach by means of clamps. The arterial cannula was connected to a narrow graduated cylinder containing the injection mass, which in turn was connected to a large reservoir of air at a pressure of 130 millimeters of mercury (Fig. 1). When the taps were opened the injection mass flowed into the arteries of the stomach, and as soon as the level of injection mass ceased to fall the injection was ended, usually in 3 to 4 minutes.

In order to demonstrate arteries and arterioles, an injection mass was used of particle size too large to enter the capillaries. Twenty per cent bismuth oxychloride, chlorbismol, was satisfactory for this purpose. When it was desired to fill the capillaries of the mucous membrane 10 per cent colloidal silver iodide was injected, followed by injection with chlorbismol to define the larger vessels.

Stomachs removed from the cadaver were injected at room temperature (19 degrees C.).

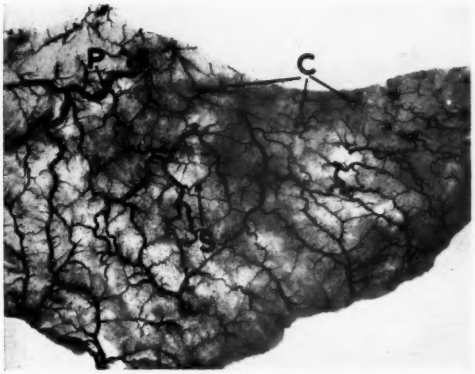

Fig. 4. Roentgenogram of the vessels of the submucous plexus in the anterior wall of the stomach showing main (*P*) and subsidiary (*S*) anastomotic channels. Note the absence of the plexus along the lesser curve, and the cut ends (*C*) of the mucosal arteries there. ×0.6.

They were used only to demonstrate the large vessels in the chains along the greater and lesser curvatures and their branches which form the submucous plexus of the stomach. For finer details and for the vessels to the mucosa, operation specimens were employed and were injected at a temperature of 37 degrees C. in a saline bath.

After injection the specimen was fixed in 10 per cent formol saline for 24 hours, then opened along the greater curve, pinned out flat, and fixation continued for another 24 hours. The specimen was now ready for roentgen examination. Roentgenograms were made of the whole stomach first; appropriate transverse frozen sections 400 microns thick were then made, and x-rayed at 20 kilovolts and 20 milliamperes by means of a soft x-ray tube with a molybdenum target and a thin beryllium window. Microradiographs of the frozen sections were made on maximal resolution film, and were capable of optical enlargement up to several hundred diameters.

Colored pigments and microdissection. Roentgenography provides a general picture of arteries, arterioles, and capillaries and so helps to define the problem. More precise and detailed information has to be sought by injecting arteries and veins with pigments of different colors, clearing the specimen to render it translucent to light, and then tracing

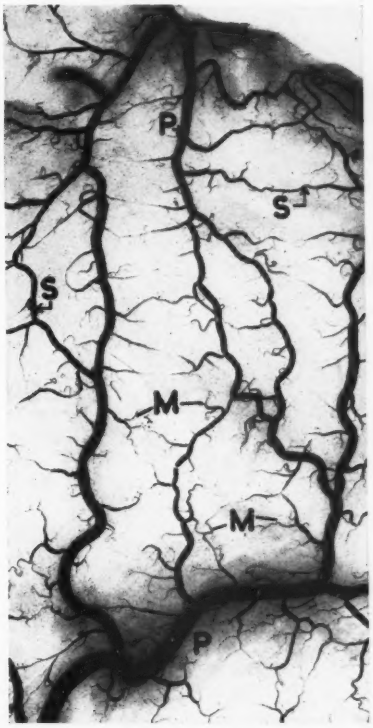

Fig. 5. Enlargement from Figure 4 of a portion of the submucous plexus in the anterior wall of the body of the stomach. *P*, main anastomotic channels; *S*, subsidiary anastomotic channels; *M*, mucosal arteries. ×2.

the course of individual vessels through the stomach wall by patient dissection under the dissecting microscope.

For this purpose the injection mass consisted of 10 per cent gelatine in saline or human plasma, to which was added 5 per cent of colored pigment, red or blue. The mass flowed readily (at 37 degrees C.) into the capillaries. To prevent capillary filling and so permit easier study of the larger branches, 20 per cent of rice starch granules, 20 microns in diameter (Scharrer 1940) was added to the injection mass in certain experiments.

Operation specimens were used for these injections, the vessels cannulated, and injection carried out at a temperature of 37 degrees C. in a saline bath using the methods and apparatus illustrated in Figure 1.

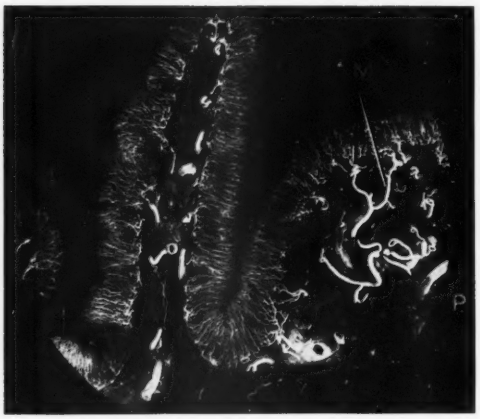

Fig. 6. Roentgenogram of the vessels in a fold of mucosa from the posterior wall of the body of the stomach. Transverse section 400 microns. *P*, submucous plexus; M, mucosal arteries. ×5.3.

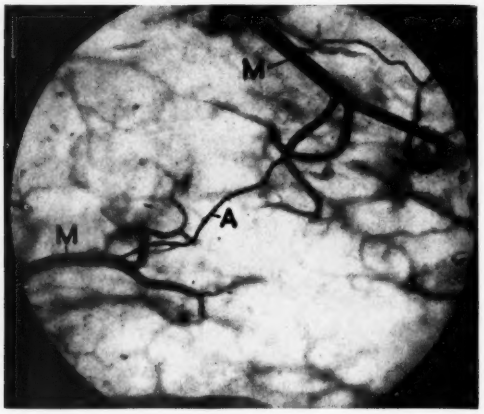

Fig. 8. Black and white print from a colored preparation showing an anastomosis (*A*) between two mucosal arteries (*M*) on the under aspect of the muscularis mucosae, in the anterior wall of the body of the stomach. ×42.5.

To fill all vessels including the capillaries of the mucosa red gelatine solution was injected by the arterial cannula at a pressure of 130 millimeters of mercury until all blood had flowed out of the specimen through the venous cannula and red injection began to appear. The arterial injection was then stopped, and injection through the venous cannula begun at a pressure of 80 millimeters of mercury with blue gelatine solution containing 20 per cent rice starch granules. The blue mass pushed back the red arterial injection as far as the capillaries, but could not enter the capillary channels because of the large rice granules. After 3 to 4 minutes the venous injection was stopped, the cannulated vessels ligated, and the specimen fixed in 10 per cent formol saline in routine manner.

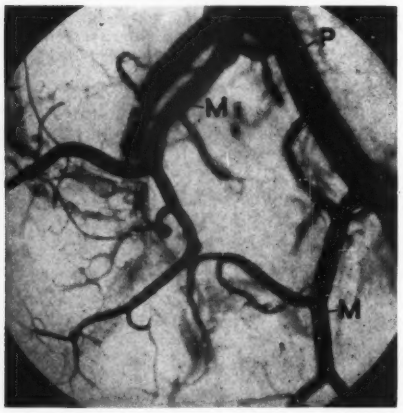

Fig. 7. Black and white print from a colored transparency of a specimen in which arteries and veins are injected with colored dyes. *P*, main anastomotic channel submucous plexus. *M*,*M*, mucosal arteries crossing the submucosa and dividing as they approach the muscularis mucosae. Note the large size of the accompanying vein. ×17.

To fill all the vessels except the capillaries the vessels of the stomach were washed out with isotonic saline at 37 degrees C. from the arterial to the venous cannula at a pressure of 130 millimeters of mercury until no more blood emerged. The arterial and venous cannulas were then injected simultaneously with red and blue injection solution respectively, each containing 20 per cent rice starch granules. Arterial injection was carried out at 130 millimeters of mercury and the venous injection at a pressure of 80 millimeters of mercury. Injection was continued until, in 3 to 4 minutes, the masses ceased to flow; the cannulated vessels were ligated and the specimen fixed. Subsequent examination showed in all instances that arteries and veins were well filled, down to the capillaries.

After 24 hours the specimen was opened along the greater curve and the muscle coat

Fig. 9. Black and white print from a colored preparation showing the network of anastomosing channels (*D*) on the glandular aspect of the muscularis mucosae from which the capillaries of the mucosa arise. Anterior wall of the body of the stomach. Note two different sizes of capillaries in the mucosa. ×62.

dissected off the underlying mucosa and mucous membrane, revealing the plexus of large vessels and its branches in the submucous connective tissue. This extensive sheet of submucous and mucous tissue was now cleared by immersion in the following solutions:

7 days in 2 per cent potassium hydroxide
7 days in 20 per cent glycerine
7 days in 40 per cent glycerine
7 days in 60 per cent glycerine
7 days in 80 per cent glycerine
7 days in pure glycerine

The specimen kept indefinitely in pure glycerine.

When the clearing process was completed the specimen was dissected on the flat stage of a dissecting microscope; by transmitted light the injected vessels were clearly visible. In this way it was possible to follow the precise arrangement and distribution of the arteries and veins in the submucosa and mucous membrane. Final details of the capillaries in the mucosa were obtained by making frozen sections of the injected material; these were cleared on the slide, mounted, and then photographed.

RESULTS

THE VESSELS OUTSIDE THE STOMACH

There is nothing to add to the accepted anatomy of the gastric blood vessels outside the stomach wall. The stomach lies within a network of large anastomosing vessels; on the lesser curve run the right and left gastric

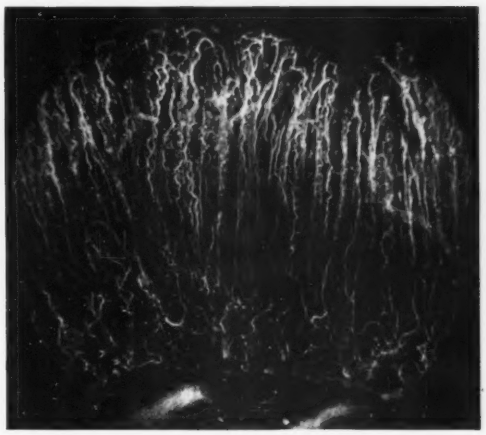

Fig. 10. Roentgenogram of the capillaries of the mucous membrane, taken from the anterior wall of the body of the stomach. Transverse section 400 microns. Observe the vertically running larger vessels and the smaller capillaries ramifying in between. ×24.4.

arteries and veins, and along the greater curve is the gastroepiploic chain, reinforced at the left extremity by the vasa brevia. The large vessels of the gastric chains have extensive connections, through branches easily visible to the naked eye, with many arteries in the upper abdomen, particularly the splenic and superior mesenteric. The connections can be readily demonstrated in the cadaver by injection of the left gastric artery with a colored dye, after ligation: (1) of the celiac axis (to prevent backflow into the aorta), (2) the left gastric stem proximal to the point of injection

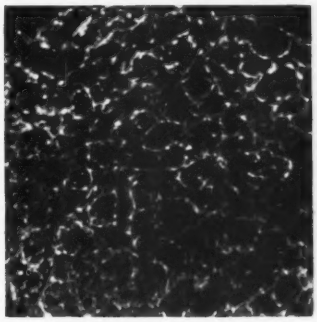

Fig. 11. Roentgenogram of the surface loops of the capillaries, taken from the posterior wall of the body of the stomach. Tangential section 200 microns. ×37.6.

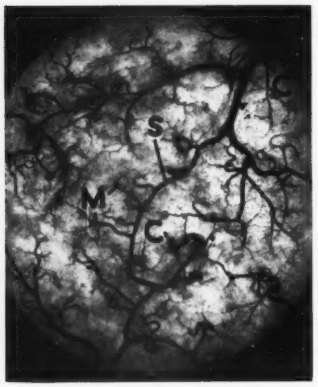

Fig. 12. Black and white print of a colored preparation, showing the vessels of the submucous plexus in the anterior wall of the pyloric antrum. *C*, cut ends of arteries as they pierce the muscle; *S*, anastomoses between ends of these arteries; *M*, mucosal arteries. Compare with Figure 5. ×2.

(to prevent backflow into other branches of the celiac axis), (3) the hepatic artery distal to the point of origin of the gastroduodenal artery (to prevent injection fluid passing on to the liver). As the injection proceeds the stomach vessels fill, but simultaneously dye passes into the splenic artery to fill the spleen, and into the superior mesenteric to fill the enormous vascular area of small bowel and proximal colon. More than half a liter of injection mass can be introduced through the left gastric artery (at a pressure of 130 mm. Hg) to the early bewilderment of the experimenter; but the anastomosing channels are plain to see, especially around the head of the pancreas. The impression is created that although in the abdomen named arteries pass to their usual formal destinations, the whole of the supply to the stomach and bowel might be regarded as one large latticework of vessels, which are fed at fairly constant points by the named arteries and which could permit blood flow to be directed toward or away from any particular area if suitable conditions of vessel control existed.

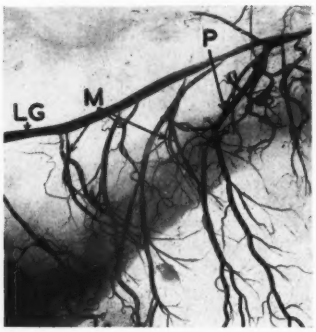

Fig. 13. Roentgenogram of the vessels supplying the lesser curve region. *LG*, left gastric artery; *P*, main supply channels of submucous plexus; *M*, mucosal arteries on lesser curve. ×1.

As the left gastric artery turns down along the lesser curve of the stomach it usually divides into two branches, one running on the anterior and the other on the posterior aspect of the lesser curve, both vessels lying within the limits of the lesser omentum. One or other of these branches, usually the anterior (but sometimes both), joins directly with the small right gastric artery to complete the lesser curve chain.

The gastroepiploic chain extends from the lower border of the first part of the duodenum, where the duodenum becomes adherent to pancreas, to a point on the greater curve just distal to the lower end of the spleen. More proximal to this the vasa brevia supply the fundus area of stomach.

MUCOSAL SUPPLY

Arteries. The anterior and posterior walls of the body of the stomach have a precisely similar vascular arrangement, but there are certain differences in the pyloric antrum and along the lesser curve (Fig. 2). They will therefore be described separately.

1. Anterior and posterior walls of the body of the stomach.—Branches arise at intervals of about 1 centimeter from the arterial chains on the greater and lesser curves, and pass on to the surface of the stomach. Those from the gastroepiploic chain penetrate the muscle coats of the stomach about 2 centimeters from the greater curve (Fig. 3). The branches from the lesser curve chain pass obliquely across the stomach toward the pylorus, piercing the muscle coat about 1.5 centimeters from the line of the curvature.

Having pierced the muscle coats the branches proceed toward each other in the submucous

layer, and, without any loss in size, form an anastomosing network—the submucous plexus (Figs. 3, 4, and 5). In the fixed specimen these vessels are about 200 microns in diameter, and the loops of the plexus are further connected by cross-anastomosing channels about 150 microns in cross-section, which lie a little deeper in the submucous tissue. The presence of this extensive plexus of small arteries in the submucosa explains the extreme vascularity of this layer when involved in an acute ulcer or sectioned at operation. The plexus is continuous over the whole of the anterior and posterior walls, and from it arise the arteries supplying the mucous membrane.

The blood supply of the mucosa arises as a series of separate branches from the main or subsidiary channels of the submucous plexus (Fig. 5). Each branch takes an oblique course across the submucosa toward the muscularis mucosae (Fig. 6). On the under aspect of this tissue each mucosal artery is connected with its neighbor by a slender anastomosing channel about 50 microns in diameter (Fig. 8). The mucosal artery then breaks up into 3 or 4 branches which twist and coil upon each other, before piercing the muscularis mucosae (Figs. 7 and 8). About 90 to 120 of these branches are to be found perforating each square centimeter of the muscularis mucosae (Fig. 15). On the upper, glandular, aspect of this muscle layer the branches freely anastomose with each other to form a network of channels from which the characteristic vessels of the mucous membrane arise (Fig. 9).

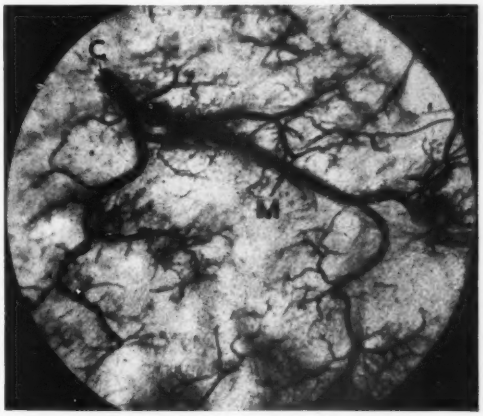

Fig. 14. Black and white print of a colored preparation, showing a mucosal artery (*M*) of the lesser curve, from its origin (cut end *C*) outside the wall of the stomach to its terminal branches. Note the absence of a submucous plexus of vessels. ×17.85.

The vessels of the mucosa consist of leashes of large capillaries, about 20 microns in diameter, which run vertically through the mucosa, appearing almost to fill its substance (Fig. 10). From the vertical vessels smaller capillaries arise (8 microns) which ramify among the glands like the arborizations of a tree, each spread of branches joining with

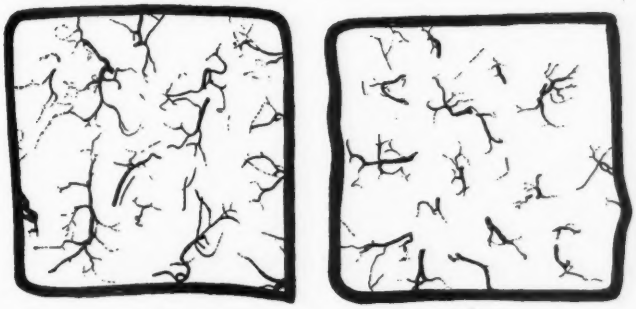

Fig. 15. Camera Lucida drawing of the mucosal arteries close to the muscularis mucosae, taken from a colored preparation. The greater part of the submucous tissue has been removed, and the mucosal arteries sectioned close to the point where they divide into their terminal branches. The side of the marked square is 0.5 centimeter in length. a, Lesser curve region; b, anterior wall of the body of the stomach. Note the similar number of mucosal branches in each square. ×8.4.

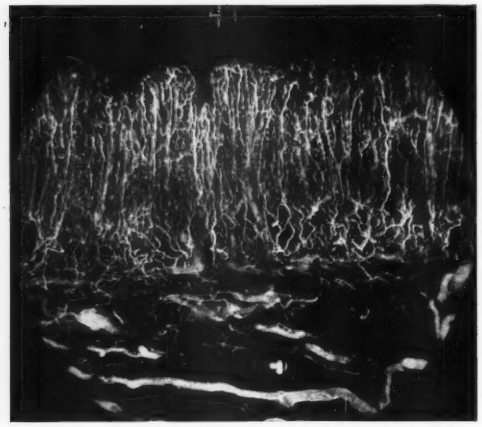

Fig. 16. Anterior wall. ×14.45.

Figs. 16, 17, 18. Roentgenograms of the vessels of the mucosa, taken from a continuous strip of anterior wall, lesser curve, and posterior wall of the body of the stomach, showing the similar vascular pattern. Transverse sections 400 microns.

adjacent capillaries and forming at the surface larger capillary loops about 15 microns in diameter, around the openings of the glands (Fig. 11).

2. Anterior and posterior walls of the pyloric antrum.—The branches from the arterial chains on the two curvatures pass obliquely across the outer surface of the pyloric antrum and divide before piercing the muscle coats to reach the submucosa. In that layer the vessels break up into 3 or 4 smaller branches, 100 to 150 microns in diameter, which anastomose with neighboring branches to form a submucous plexus of smaller size and extent than that found in the body of the stomach (Fig. 12), the vessels corresponding in diameter to the smaller cross-anastomotic channels of the main submucous plexus. From the limbs of this plexus the mucosal arteries arise and have the same distribution as mucosal arteries in the body of the organ, anastomosing as they approach the muscularis mucosae and supplying the mucosa in the usual manner. The vascular pattern of the pyloric antrum is thus the same as in the anterior and posterior walls of the stomach body, except that the submucous plexus is formed by rather smaller arteries (Fig. 12). The course of the mucosal arteries, the number of branches per square centimeter of mucosa, and the arrangement of vessels in the mucous membrane are indistinguishable from the conditions found in the body of the stomach.

3. Region of the lesser curve.—The branches of the right and left gastric arteries destined for the supply of the anterior and posterior walls pierce the muscle coats of the stomach about 1 to 2 centimeters from the line of the lesser curve, as has been described. The tissue along the lesser curve and for 1 to 2 centi-

Fig. 17. Lesser curve. ×14.45.

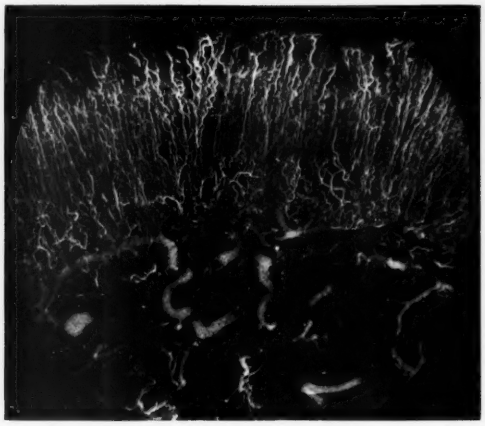

Fig. 18. Posterior wall. ×14.45.

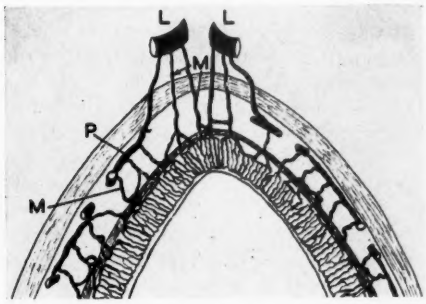

Fig. 19. Diagram illustrating the origin of the mucosal arteries in the lesser curve and in the anterior and posterior walls. *L*, left gastric arteries; *P*, submucous plexus; *M*, mucosal arteries.

Fig. 20. Black and white print of a colored preparation showing the large veins (*V*) draining the mucous membrane. ×23.6.

meters on either side of it is supplied by slender vessels about 60 to 100 microns in diameter which arise from the right and left gastric arteries and may be connected by anastomotic branches before piercing the muscle coats to reach the submucosa (Fig. 13). They then traverse the submucosa toward the muscularis mucosae without the formation of a submucous plexus. These vessels are the mucosal arteries; they arise not from a submucous plexus in the stomach wall, as is the case in the rest of the stomach, but directly from the arterial chain within the lesser omentum outside the stomach, and so have to pierce the muscle coats of the stomach in their long passage from origin to distribution (Figs. 14 and 19). Approaching the muscularis mucosae the adjacent mucosal arteries anastomose with each other, or, where the lesser curve merges with the anterior and posterior walls, with the corresponding mucosal artery from the submucous plexus of those walls.

Reeves (1920) and Djørup (1922) noted the presence of much smaller anastomosing branches in the lesser curve region, compared

Fig. 21. ×23.6.

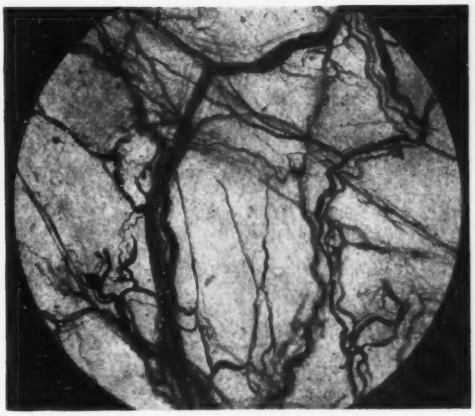

Fig. 22. ×16.45.

Figs. 21 and 22. Black and white reproduction of a colored transparency, showing the complicated series of loops of the extensive plexus within the submucous connective tissue.

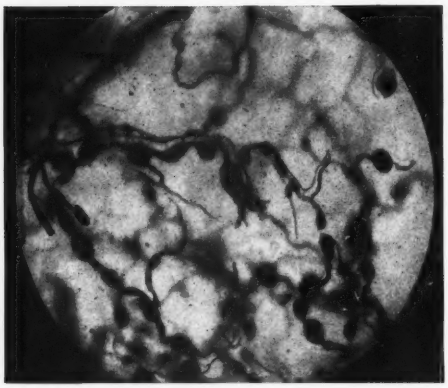

Fig. 23. Black and white print of a colored preparation, showing venous saccules in the connective tissue plexus. Note further loops in depth out of focus in the center of the field. ×11.5.

with the large communicating channels (of the submucous plexus) in the anterior and posterior walls, but the significance of this observation does not seem to have been made clear. There is no submucous plexus in the lesser curve region; the small communicating channels seen within the submucosa of the lesser curve are the fine anastomotic branches which connect mucosal arteries in all parts of the stomach. It is possible that branches which connect the mucosal arteries of the lesser curve outside the stomach wall (Fig. 13) correspond with the connecting channels of the submucous plexus which exist in the body of the stomach.

The distribution of the mucosal arteries in the lesser curve is precisely the same as in other parts of the stomach. The artery divides on the underaspect of the muscularis mucosae into three or four small twisting branches, which then pierce this muscle layer and form an anastomosing channel on its glandular aspect before splitting up into leashes of capillaries, characteristic of gastric mucosa. The number of vessels piercing a square centimeter of muscularis mucosae in this region is the same as in a similar area from the anterior wall (Fig. 15). Except that the mucosa of the lesser curve is sometimes a little less thick than is the mucosa of the anterior and posterior walls, there is no demonstrable anatomical difference between it and the rest of the gastric mucosa, in regard to the number or size of the mucosal arteries supplying it, or in the richness of the capillary network within it, or in the pattern of the capillary vessels (Figs. 16, 17, and 18). Provided that artefacts or errors in injecting technique are avoided, it is not possible to distinguish between pieces of mucosa from the lesser curve or other parts of the stomach on the basis of their vascular structure. The anatomical differences in the arrangement of blood vessels in the lesser curve region consist of an extragastric origin of the mucosal arteries and an absence of a submucous plexus. The mucosal pattern is indistinguishable. The comparison is shown schematically in Figure 19.

Veins. Except in the mucous membrane, the veins of the stomach wall correspond to the arteries, differing only in their larger size (Fig. 7). In the mucosa blood from the surface capillaries is collected into large venules 90 to 90 microns in diameter which lie close to the surface (Fig. 20). Several venules unite

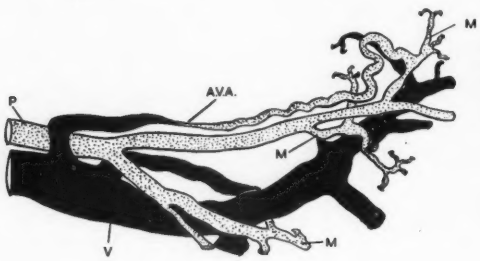

Fig. 24.

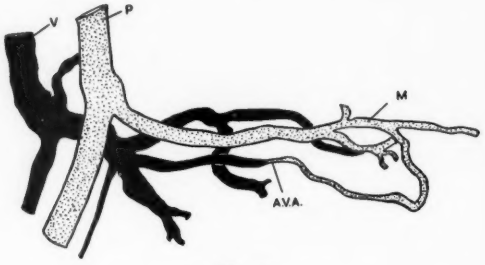

Fig. 25.

Figs. 24 and 25. Projection drawing of a color transparency of an arteriovenous anastomotic loop in the submucosa. *P*, Submucous plexus; *M*, mucosal artery; *V*, mucosal vein; *A.V.A.*, arteriovenous anastomosis. ×20.

to form a mucosal vein which runs vertically through the mucosa and pierces the muscularis mucosae to enter one of the large veins accompanying the mucosal arteries there. The mucosal veins in turn drain into the wide venous channels of the submucous plexus, except in the lesser curve region where the mucosal veins have a corresponding course to the long mucosal arteries and pierce the muscle coats of the stomach before entering the venous chain outside the stomach walls, without the intervention of a submucous plexus.

THE CONNECTIVE TISSUE PLEXUS

There is throughout the stomach a layer of connective tissue of considerable thickness lying between the muscle coats and the muscularis mucosae. It contains the ramifications of the submucous plexus and the mucosal arteries already described. In addition it is filled with a vast network of small arteries and veins, varying in diameter from 100 microns to capillary size, which form a complicated series of loops in the interstices between the limbs and branches of the submucous plexus. The loops fill the substance of the mucosa and vary in number according to the thickness of that layer, up to 6 loops being visible in the thickest (Figs. 21, 22).

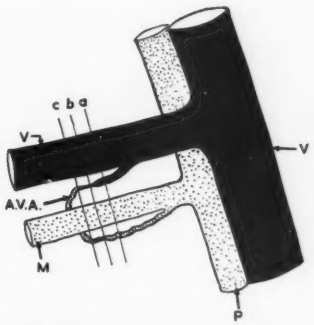

Fig. 26. Diagram of the arteriovenous loop from which serial transverse sections were cut, three of which (*a*,*b*,*c*) are shown in Figures 27 to 29. *P*, submucous plexus: *M*, mucosal artery; *V*, mucosal vein; *A.V.A.*, arteriovenous loop.

The vessels are usually paired artery and vein, the vein being of larger size. They arise from the limbs of the submucous plexus, are expended entirely in the substance of the submucosa, and do not penetrate the muscularis mucosae to reach the mucous membrane. The loops freely communicate with each other, and with the vessels of the muscle coats, but have no connection with the submucous plexus after their point of origin or with the mucosal arteries and veins. In places where the vessels of the connective tissue plexus lie adjacent to

Fig. 27.

Fig. 28.

Fig. 29.

Fig. 27. Transverse section (12 microns) at *a*, Figure 26. Note the thin wall of the venous portion of the arteriovenous channel (*A.V.A.*); *V*, mucosal vein. Stained hematoxylin and eosin. ×286.

Fig. 28. Transverse section (12 microns) at *b*, Figure 26. Note the thick wall of the narrowed portion of the arteriovenous channel, *A.V.A.*, due to large cells in the wall which also project into the lumen; *V*, mucosal vein. Stained hematoxylin and eosin. ×286.

Fig. 29. Transverse section (12 microns) which was taken at *c*, Figure 26. Note the thinner wall of the arterial part of the arteriovenous channel *A.V.A.*; *V*, mucosal vein: *M*, mucosal artery. Stained hematoxylin and eosin. ×286.

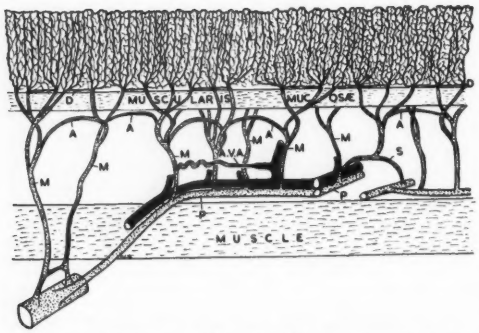

Fig. 30. Diagram of the vascular arrangement in the stomach wall. On the extreme left is shown the lesser curve with mucosal arteries *M* arising from the left gastric artery outside the stomach wall. On the right the pattern as seen in anterior or posterior wall annotated as before. In the center an arteriovenous anastomosis in relation to the other vessels.

the limbs of the submucous plexus, they send many cross-anastomosing branches in front of and behind the large arteries and veins, forming a complicated ladder pattern around these main channels.

The veins frequently show small dilatations, especially at the bends of the loops and at points of junction with other veins. In occasional areas of the anterior and posterior walls of the body of the stomach the dilatations are especially noticeable, forming multiple venous saccules not unlike varices (Fig. 23).

The outstanding features of the connective tissue plexus are its great extent and richness, and—in spite of its multitude of branches—its isolation from the mucosal supply. The mucosal arteries pass through the complicated loops and whirls of the connective tissue plexus, requiring much dissection to make clear their course; at no point has a mucosal artery been seen to communicate with a branch of this connective tissue plexus. The extent of the connective tissue plexus, its fineness of vessels, rigid confinement to the submucous layer, and lack of communication with the mucosal vessels provide as yet no adequate clue to the function of this plexus in the stomach wall.

ARTERIOVENOUS ANASTOMOSES

Enough is known about arteriovenous anastomoses to expect their presence in all tissues in which activity is phasic and great changes in blood flow occur. In general there are two main anatomical types: the first, a complicated knot of vessels or "glomus," whose walls are characterized by an epitheloid type of cell replacing the muscle cell in the tunica media and controlling the anastomosis by its swelling or shrinking. The second type exists as a more or less direct channel, usually of sinuous form, which may be controlled by muscle cells in the vessel wall. The monograph by Clara (1937) presents the available knowledge up to that time.

de Busscher (1948), by means of reconstruction of serial sections of human stomach wall, described arteriovenous anastomoses of both types in the submucous and muscle layers, the "glomus" form predominating. The experiments of Barclay and Bentley (1949) inferred the presence of functioning arteriovenous shunts in the human stomach, as demonstrated by changes in oxygen saturation of venous blood from the stomach under different conditions, and by microarteriography. It was necessary to proceed further, and to demonstrate the shunts in an unambiguous way by an objective anatomical technique. The method of double injection of the vessels described is particularly apt for such an investigation, for in the injected and cleared stomach wall the vessels can be clearly seen by transmitted light, and any arteriovenous anastomosis revealed in its intact state by microdissection. Our results show that arteriovenous anastomoses of the direct sinuous type are in fact present in considerable numbers in the human stomach wall, but we have not been able to find in the submucosa any evidence of the complicated glomus form of anastomosis described by de Busscher.

The arterial end of the arteriovenous channel is usually a branch of a mucosal artery, though it occasionally arises direct from a main limb of the submucous plexus; it takes a long winding course through the submucosa, exhibiting several bends and turns, until it narrows and joins a vein, which shortly widens and opens into a mucosal vein or into a vein of the submucous plexus (Figs. 24 and 25).

These direct channels show considerable variations in length and direction. Some take

a simple circular course in the submucosa, others follow a more or less straight direction except for occasional sinuous waves; sometimes the course is short, the small artery doubling back on itself to enter the corresponding mucosal vein. In most instances, however, the arterial part of the vessel is long and winding and may approach or enter the substance of the muscularis mucosae before opening into a vein. The venous channel may join the arterial branch at an acute or right angle, but more often the two vessels continue straight into each other.

At the point of junction the vessel narrows, and it is here where the red arterial injection is seen to meet the blue venous mass. The narrow part is quite short, about 1 to 2 millimeters in length, and in the fixed cleared operation specimen the lumen at this point may be almost occluded (Fig. 25). Elsewhere the anastomotic channel is not less than 30 microns in diameter, but evidence will be given later to suggest its much larger size, up to 140 microns in life.

Serial transverse sections of an arteriovenous channel, from its arterial origin through the narrowed portion into the wide vein, show a considerable increase in the thickness of the vessel wall along the whole length of the constricted part. The thickening is due to the presence of large cells which surround the vascular channel, and here and there project into the lumen so as to narrow it to a mere slit (Figs. 26, 27, 28, and 29). The cells, in spite of the previous treatment with potassium hydroxide and glycerine, can be recognized as belonging to the musculoepithelial type of cell specified by Clara as occurring in some types of arteriovenous anastomoses.

There appears to be little difference in the distribution of the arteriovenous channels in the different parts of the stomach. It is usually possible to find a shunt arising from each mucosal artery, whether on the lesser curve or in the anterior or posterior wall, though there is less constancy in the occurrence of arteriovenous communications arising directly from the limbs of the submucous plexus. The shunts are of smaller size than the mucosal arteries from which they arise, which suggests that they may never have to take the maximum volume of blood which can flow to the mucous membrane.

Summary

The mucous membrane of the stomach has a rich blood supply, consisting of arborizing leashes of capillaries which appear to fill almost completely the glandular layer, like a vascular sponge. The arrangement of vessels in the mucosa is the same in all parts of the stomach.

The capillaries of the mucosa are supplied by long mucosal arteries, about 120 microns in diameter (in the fixed specimen), which cross the submucosa obliquely to penetrate the muscularis mucosae and reach the glandular layer. In the anterior and posterior walls of the body of the stomach these mucosal arteries arise from an extensive plexus of large vessels in the submucosa which in turn is supplied by branches from the arterial chains on the greater and lesser curves. In the pyloric antrum there is a similar arrangement except that the plexus in the submucosa consists of smaller vessels.

In the region of the lesser curve the mucosal arteries do not arise from a plexus of vessels within the stomach wall, but have their origin outside the stomach, directly from the right and left gastric arterial chain. The slender vessels pierce the stomach wall to enter the submucosa which they traverse in an oblique manner, without the formation of a submucous plexus, to reach the mucosa and supply it in a manner similar to that seen in the rest of the stomach wall. The vascular arrangement in the lesser curve region gradually merges with that in the anterior and posterior walls.

There is wide connection of the mucosal arteries throughout the stomach, by their free anastomosis as they approach the muscularis mucosae and again on the glandular aspect of that muscle. The freely anastomotic nature of the vessels of the stomach wall is perhaps its most notable feature. There are no anatomical end-arteries. The mucosa lies within a large vascular network consisting of anastomosing mucosal arteries and the submucous plexus of large vessels, in communication with

the arterial chains on the greater and lesser curves. Whatever the physiological mechanism of control may be, channels exist capable of bringing large quantities of blood to the mucosa or of transferring blood from one point to another in the stomach wall.

The shift of blood in the stomach wall is further facilitated by a mechanism for short-circuiting the mucosal arteries directly into the veins. These direct arteriovenous channels, up to 140 microns in diameter, commonly arise from the mucosal arteries, and their presence suggests a rapid means of directing blood into or away from the mucous membrane, by purely local action involving relatively few vessels. The general arrangement of the vascular pattern in the stomach wall is summarized in Figure 30.

NOTE ON FLOW THROUGH THE ARTERIOVENOUS ANASTOMOSES IN THE STOMACH WALL

The arrangement of blood vessels in the stomach wall suggests that total blood flow in the stomach is made up of several components. There is the circulation within the submucous plexus; the flow through the mucosal arteries to the mucous membrane, and the varying proportion of that flow which passes by the arteriovenous anastomoses; the passage of blood through the complicated network of the connective tissue plexus within the submucosa; and, feeding all these channels, the circulation through the branches to the stomach of the extragastric chains on the greater and lesser curvatures.

It is as yet not practicable to study any of these components, or even total blood flow to the stomach, in the intact man; but by using the distal two-thirds of human stomach excised at operation for duodenal ulcer, it is possible by laboratory methods to determine the size of the arteriovenous anastomoses in the living state, and to make preliminary inquiry into the passage of circulating fluid through these channels.

By employment of standard physiological techniques the vessels of the excised stomach may be perfused with eserinized human plasma, and the rate of flow of perfusate may be measured. Under suitable conditions the stomach remains healthy and active for at least 8 hours (the longest period we have studied), as judged by the continuous secretion from the mucosa, and by the response of the muscle coats and the blood vessels to circulating drugs. If small glass spheres are introduced into the arterial inflow (Prinzmetal *et al.*, 1948)—spheres about 40 to 140 microns in diameter, too large to pass by capillary channels—they can be recovered in considerable numbers from the venous outflow. The number of spheres found in each milliliter of perfusate collected from the vein is taken as an index of flow through the shunts at that particular time. It is found that the flow of spheres through the shunts varies considerably under different conditions, such as stimulation of nerves in the stomach wall or the addition of adrenalin to the perfusing fluid, conditions which can be constantly repeated with uniform results.

The spheres injected into the arterial inflow are from 40 to 200 microns in diameter, average size 120 microns, and when a test dose is injected spheres can be recovered from the venous outflow of 40 to 140 microns in diameter (average 100 microns), spheres larger than 140 microns being retained. The number of spheres passing varies according to the conditions of the experiment, but the range of size as expressed in the mean diameter or in a size-distribution curve varies little. Moreover, it has not been possible to modify, by physical or pharmacological stimulation of the stomach, the proportion of large or small spheres which pass through the shunts. It is concluded therefore that variations in the number of spheres passing are not due to alterations in diameter of already functioning arteriovenous anastomoses, but to increased flow through shunts already functioning, or to the bringing into use of previously nonfunctioning anastomoses.

Electrical stimulation of a nerve bundle accompanying the left gastric artery along the lesser curve causes a marked decrease in the rate of perfusion, and a simultaneous increase in the outflow of spheres. The same result is obtained when adrenalin (10 micrograms per milliliter) is added to the perfusing plasma. That is, the flow through the shunts as judged by the outflow of glass spheres is

much increased, while the total flow through the stomach vessels is considerably reduced. The precisely opposite effect is obtained in some experiments when acetylcholine (10 micrograms per milliliter) is added to the plasma—the total flow through the stomach vessels is markedly increased, but the flow through the shunts as measured by the passage of glass spheres is much reduced.

CONCLUSION

From these early experiments all that can be concluded is that the arteriovenous anastomoses demonstrated by microdissection of the stomach wall are functioning entities and that their maximum size is about 140 microns. Although the number of spheres which pass varies according to many conditions, the proportion of small and large spheres in the outflow remains constant; it appears therefore that the shunts do not maintain intermediate positions of opening, but remain either open or shut. Conditions which reduce the total rate of flow through the stomach vessels produce an increased flow through the shunts; and conversely, conditions which increase the rate of flow through the stomach vessels are associated with a decreased flow through the arteriovenous anastomotic channels.

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THE NEUROVASCULAR MECHANISM OF THE MUCOUS MEMBRANE OF THE STOMACH

H. B. BENJAMIN, M.D., M.Sc., Milwaukee, Wisconsin

FOR complete obstruction of end-arteries, a large amount of interference must occur, such as that caused by a large thrombus or atherosclerotic plaque or plaques—large for the size of the vessel.

Because of the vortex it sets up, as a rule, the linear blood pressure in a true end-artery is sufficient to force some blood through; whereas, in areas of the large anastomosis, the blood can be channeled around the thrombus or occluding plaque. In the end-artery the linear pressure may either break up the fresh thrombus or canalize the old one. In the anastomotic vessels the blood can flow around the thrombus and so fail to disturb the clot. This action allows the clot to pyramid to undue size. The severity of the reaction to the thrombus may be out of proportion to its size. The symptoms are more than likely due to the reflex sympathetic vasoconstriction of associated vessels. This type of response is known as group reaction (2). As the vagus and sympathetic systems contain afferent and efferent fibers the normal vascular response depends upon an equilibrium between these two systems (10–3). This type of neurovascular mechanism is especially active in the lungs.

For some time studies at this institution on the neurovascular mechanism of the stomach and duodenum and the pattern of the large and small blood vessels in these organs have demonstrated this selective response (4) (Figs. 1 and 2). Stimulation of the distal stump of the cut right vagus showed a loss of the gross vascular pattern in the pyloric area of the injected stomach, as shown in Figures 5, 6, 7, and 8. Because of the work of Wolf and our own findings, the study of the neurovascular reactions in the mucous membrane of the stomach was a natural sequence. The anatomical and x-ray studies of the gastric and duodenal mucous membrane of injected stomachs showed that these folds were closely associated with large blood vessels and that they became flat or thick, depending upon gastric contractions and the regional vascular state (6). Figure 7 shows this type of reaction. Although the large vessels in the loose areolar vascular highway are stuffed with contrast material, the small blood vessels in the mucous membrane are barely visible. Contrast this with Figures 3 and 4. By using a technique of microarteriography as developed by Barclay (1, 2) Key was able to demonstrate the change in the vascular pattern in the mucous membrane but, to a greater extent, in the submucosal layer.

From the Department of Anatomy, Marquette University School of Medicine.

METHODS AND MATERIALS

Human stomachs removed at postmortem examinations were injected with 50 milliliters of 20 per cent neosilvol, followed by 50 to 100 milliliters of a solution of 10 per cent bismuth oxychloride. As neosilvol is a colloidal radiopaque material, it passed from the arterial to the venous side; whereas, bismuth oxychloride, because of its particle size, remained on the arterial side. The injection method simulated normal heart action and the pressure used was close to the normal blood pressure in man, 120 to 150 millimeters of mercury. When postmortem material was used the stomach was removed shortly after death and placed in physiological saline at body temperature. The injection completed, the specimen was placed in 10 per cent neutral formalin for 12 hours. The specimen was opened by cutting along the greater and lesser curvatures and a routine x-ray film was then taken.

The same method and technique were used in the study on dogs' stomachs. When a stomach was to be stimulated, the dog was put to sleep with intraperitoneal nembutal (1 c.c. for each 5 lbs. weight) and the right chest was entered through an intercostal space. The right vagus was then isolated, clamped, and

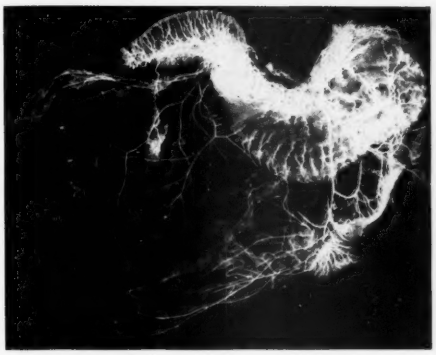

Fig. 1. Ordinary roentgenogram showing effect of subdiaphragmatic stimulation of distal stump of left cut vagus. The neosilvol-india ink injection was followed by bismuth oxychloride. Injection was done through descending thoracic aorta. Stimulation was with a Goodwin stimulator. Pyloric area appears as a solid mass of vessels, whereas cardiac-fundic area shows numerous fenestra.

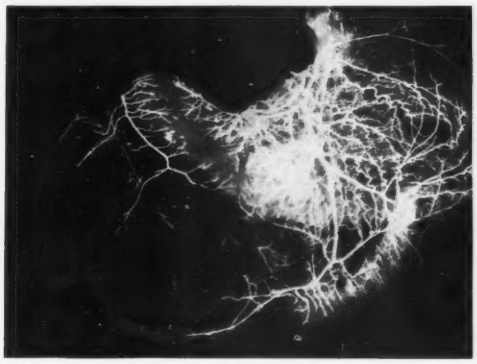

Fig. 2. Regular roentgenogram of stomach from a dog. The bismuth oxychloride was injected after the neosilvol and india ink through the descending thoracic aorta. Note the incomplete filling of the pyloric portion of the stomach and the extensive arterial venous network in the cardiac-fundic area. Stimulation of cut right vagus as stated in the text.

cut. The distal stump was then stimulated by means of a Goodwin stimulator with the use of a saw-tooth wave, frequency 20, descending phase 20 sigmas, voltage 8. After stimulation, the blood vessels of the stomach were injected through the descending thoracic aorta. The contrast material was neosilvol, followed by bismuth oxychloride. The stomach was removed from the animal, after the injection was completed, and placed in formalin. Twelve hours later, an x-ray film of the organ was taken. Then it was replaced in the formalin jar for another 12 hours. After the second fixation in formalin, blocks of tissue were cut from the pyloric end of the stomach. These blocks of tissue were then put through 50, 70, 95 per cent, and absolute alcohol. The block of tissue was then placed in a Petri dish and covered with celloidin. The celloidin was hard-

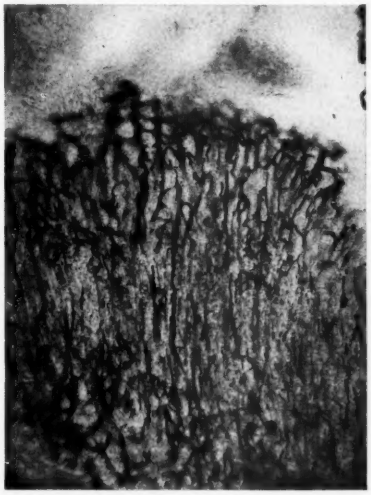

Fig. 3. Microarteriovenogram of cross section of pyloric end of unstimulated human stomach. Vessels in the mucosa are well filled and numerous loops and arborescences may be seen. Vessels extend to upper limits of mucosa.

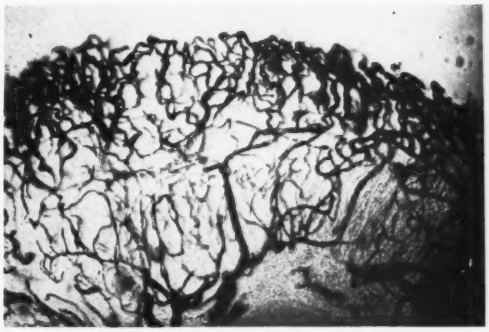

Fig. 4. Microarteriovenogram of a cross section of an unstimulated pyloric end of a dog's stomach. The vascular pattern is as extensive as its human counterpart, but the individual vessels are coarser.

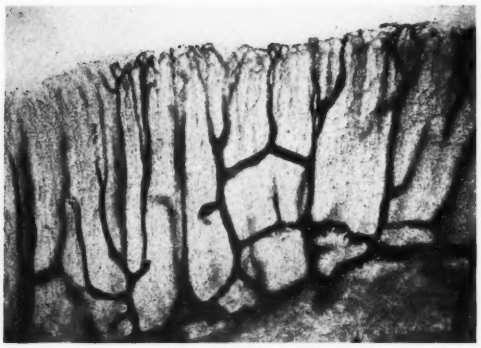

Fig. 5.

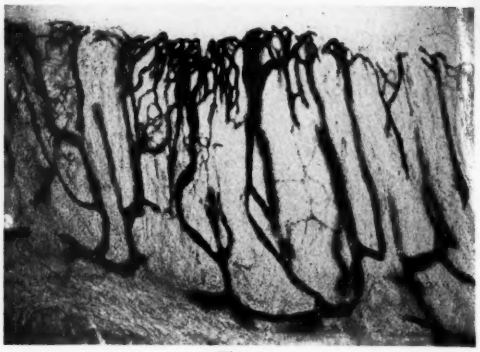

Fig. 6.

Figs. 5 and 6. Photographs of transverse sections of the pyloric end of a dog's stomach. The right vagus was cut and the distal stump stimulated. These microarteriovenograms of the mucous membrane were taken after the neosilvol-india ink and bismuth oxychloride were injected into the descending thoracic aorta. The pattern demonstrates many loops and shunts as well as coarse arborescences.

ened in chloroform. When hard, the block was cut into sections at 250 microns. These sections were placed in 95 per cent alcohol, absolute alcohol, and chloroform, then moved into xylol and, after this step, the sections were mounted on slides. Some of the sections were x-rayed by use of grenz rays. These rays have a wave length of about 2 Angström units. These sections were placed in a light tight compartment directly on a film of shellac which came in direct contact with the photographic orthopress plate. The exposure time was 1 to 2 hours, depending upon the desired detail and thickness of the specimen. For roentgenograms of specimens we used a grenz ray tube. This was constructed by using an old gas tube with a beryllium window. The focal spot was 0.5 millimeter. The sections were placed at a distance of 8 inches by the use of a light tight cone. The orthopress plates were slipped into a photographic case. These plates were used because of the fine grain of the emulsion. The films were then photo-

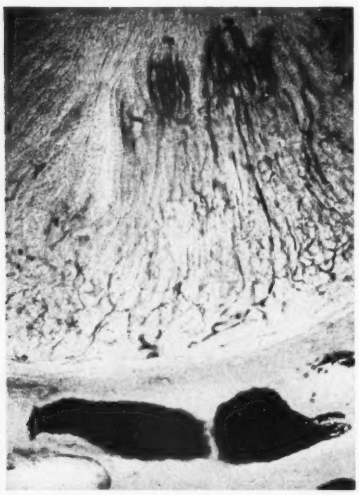

Fig. 7. Microarteriovenogram from a stimulated stomach prepared in the usual manner. The large vessels in the loose areolar vascular highway are stuffed with radiopaque material but the blood vessels in the mucosa are few in number and in some areas appear entirely absent.

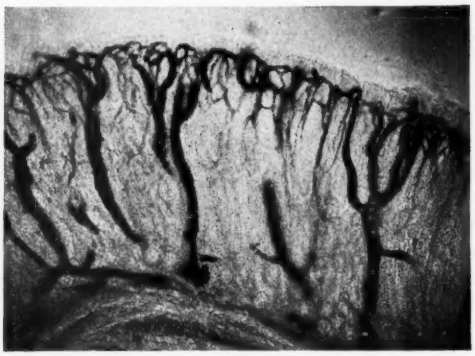

Fig. 8. Photograph of roentgenogram of a stimulated pyloric end of the stomach. The large vessels are clearly visible but the fine vessels are not demonstrated.

graphed through the conventional microscope. The magnification was 250 times while the x-rays used were 5 kilovolts. Better photographs were obtained by using routine microphotography as devised by Leo Massopust of Marquette School of Medicine.

DISCUSSION

This method of studying the microvascular architecture of the normal and stimulated stomach supports the theory that the origin of ulcers in the stomach is dependent upon a neurovascular imbalance. The fact that the stomach mucosa has an extensive anastomotic vascular network becomes obvious (Figs. 3 and 4) and, as ulcers do occur in this region, lends further support to Swindle's observations on end-arteries. Figure 1 shows the extensiveness of the vascular network in the pyloric area of the stomach, as contrasted with the stimulated stomach shown in Figure 7. The photographs of the stimulated stomachs show the marked loss of vascular pattern, and Figure 5 shows the peculiar shunting pattern that Trueta demonstrated in his study of the kidney.

SUMMARY

The vascular pattern of the unstimulated stomach and that of the stimulated stomach, as shown by microradiography and microphotography, are compared.

In the unstimulated stomach the pyloric mucous membrane contains a tremendous network of interanastomosing blood vessels that extend to the limits of the mucous membrane.

In the stimulated stomach few of these fine vessels are apparent; whereas, the large vessels arising from the loose areolar vascular highway stand out sharply. These main vessels show numerous shunting channels arranged like the steps of a ladder. It is clearly apparent how unfiltered impulses over the right vagus keep the mucous membrane in a state of anemia because of this shunting and, therefore, lead to ulcer formation.

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INTERNAL WIRE-PIN STABILIZATION FOR MIDDLE THIRD FACIAL FRACTURES

JAMES BARRETT BROWN, M.D., F.A.C.S., MINOT P. FRYER, M.D., and FRANK McDOWELL, M.D., F.A.C.S., St. Louis, Missouri

IN the stabilization of crushing fractures of the middle third of the face, internal wire-pin fixation may give excellent help. It may be used in combination with direct wiring of the zygoma to the frontal bone, through-and-through wiring fixation of the nose, interdental wiring, open elevation of the orbital borders, and with most other procedures. The internal wire in itself may suffice, except that elevation of the crushed nose and support of it on cross wires are usually necessary in instances of badly comminuted fractures. In the presence of pyramidal fractures going through the orbital borders and possibly separating the inner canthi, these areas are replaced if possible by elevation, compression, and molding before the internal wire is placed (1, 2, 4, 5, 6).

Time of operation. As soon after the accident as general and neurological conditions permit the operation should be performed. Waiting until the swelling goes down is not indicated if the best time for fixation is wanted, unless excess edema might prevent accurate approximation. After 2 weeks the fragments are so fixed as not easily to be replaced and may require forceful manipulation and separation to secure alignment. Successful replacements have been done as late as 6 weeks after the accident, but secondary reconstruction may be required if the fragments become firmly fixed out of position.

This method is applicable when the gross fragments can be brought into position by manipulation, that is, mainly in the early stages of the fracture, or in open reduction with freeing of fragments for proper alignment.

For separations of the maxilla on one side or through the palate and for loosened zygomas, the wire may produce immediate fixation and stabilization. If it can be put through a solid area into the loose fragment it may act as a cantilever support, but its main advantage is that it can hold fragments together, even if it must be passed through two loose fragments,

From the Department of Surgery, Washington University School of Medicine, St. Louis, Missouri.

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Fig. 1. (Legend on next page.)

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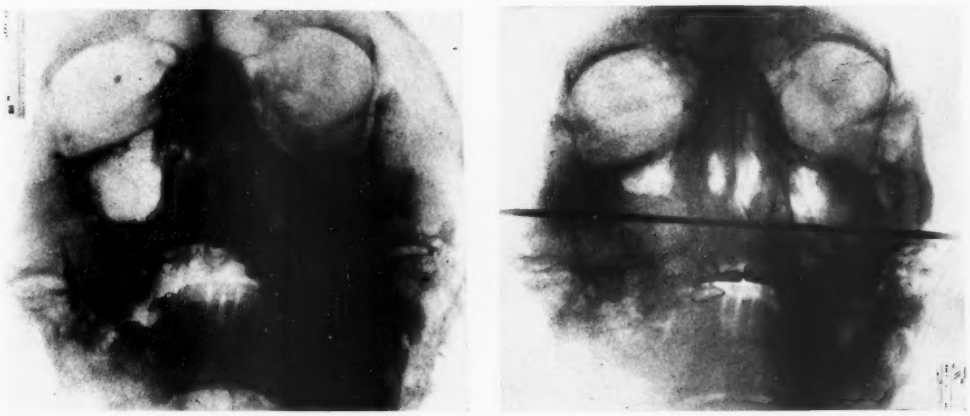

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Fig. 1. Extensive crushing injury and soft tissue damage in farm accident. There was not much stable bone left and practically no shape to the nose which was torn loose and inverted into the face. Operation was performed within 12 hours under intratracheal anesthesia. The reverse of what the accident did was carried out in "unfolding" the nose and face, elevating the left orbit, and fixing the parts with cross wires and aluminum splint for the nose and with one internal wire for the shattered pyramidal fracture and left zygomatic displacement. X-ray film shows pin in place and the zygoma restored along with the orbital border. The left eyelid is torn completely open so that the eye looks through the rent. This case is an excellent example of the necessity of early operation. To wait 10 days, as has been advised elsewhere, would result in possible eye damage and the need of multiple operations. This patient has had full restoration and rehabilitation in the one operation. No further work is necessary.

such as the two sides of a palate split open from front and back or higher in the maxilla. Pain and discomfort are relieved when the fixation is completed.

Orbital fractures. Direct elevation with a hook under the rim is considered first in orbital fractures and is applicable if impaction of the fragments will maintain the restored position (3, 7). The same impaction is necessary for other methods, such as the subtemporal approach. If the elevated orbital border will not stay up, then open reduction through the buccal fornix into the antrum is done, with an instrument to dislodge and re-

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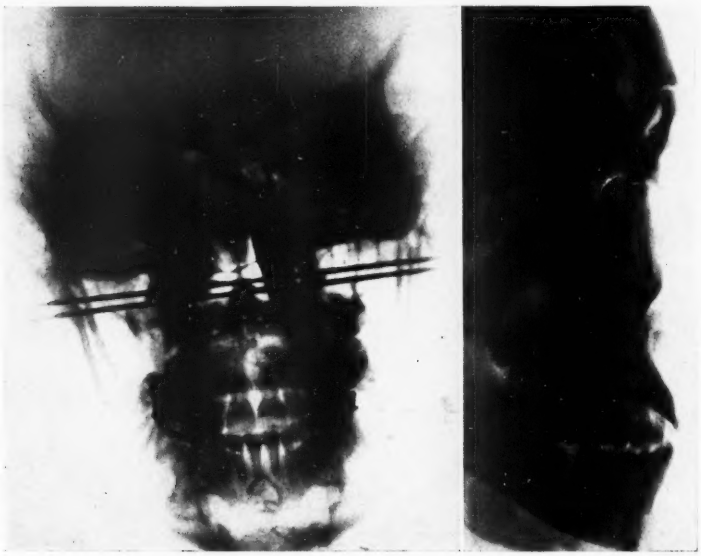

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Fig. 2. Extensive crushing of face, nose, and frontal sinus in back seat passenger traffic accident, as shown on roentgenogram. (The areas of the multiple fractures are scratched in for clearness.) She was seen after 17 days, and operation was performed under endotracheal anesthesia. Nose and face were advanced into normal position. Cross wires were used for repair of nose and 2 internal pins for pyramidal and palate fractures. This case demonstrates the ease of course for the patient without the use of extensive apparatus. Patient was out of the hospital with both internal and cross nasal wires in place, and only one operation was necessary.

place the zygomatic orbital border and the orbital floor, and, if necessary, molding from the outside with the fingers. These parts can then be held in place with iodoform gauze packing in the antrum. Open replacement and external molding into position are necessary in most instances in the presence of much displacement and comminution, but when the borders have been brought into an acceptable position the internal wire may be introduced if indicated. Preferably, it traverses one solid part of the opposite maxilla or zygoma and thus may give cantilever support to the loose fragment. The point of the wire may be

brought clear out of the cheek, and overhead elastic traction may be used temporarily on the free ends if indicated.

When the orbit is elongated and the ascending ramus of the zygoma is markedly displaced from the frontal bone, *direct wiring* may be needed, with the approach often being made through an existing wound or scar of the accident. The ascending ramus and the process of the frontal are drilled and No. 26 stainless steel wire is used for the elevation and fixation.

A block of bone like the zygoma cannot be displaced with just one fracture. It is usually knocked loose above from the maxilla and displaced down toward the antral space, or back, or out. The body of the zygoma itself is usually left intact; the comparison may be made to hitting a marble on an egg. The marble will crush the egg but will remain intact itself. These multiple fractures may require more than one plane of fixation—the lower border of the orbit may have to be raised, the ascending ramus of the zygoma which is the lateral border of the orbit may have to be fixed above to the frontal, and final stabilization may come from an internal wire.

The nose. The nose must be brought up out of the face, and if it can be packed in place and supported from the outside this may suffice. However, if it is comminuted and shattered, it may have to be brought forward in its many fragments and held in position with through-and-through wires (No. 26 stainless steel) with the ends anchored over lead plates alongside the nose.

Severe crushing injuries. There may be dozens of fractures present, and no fixed areas to give support to the face. In these instances, the face is literally "mulched" forward into position, the antra are entered through their fracture lines in the buccal fornix and are distended. The walls are carried into position with a curved clamp or elevator. Splinting is with iodoform gauze packing, 1 inch wide impregnated with balsam of Peru, within the antrum. The nose is elevated and fixed as outlined in the foregoing paragraph.

The internal wire pins are used in the most advantageous direction and find excellent adaptation in these instances. It is important

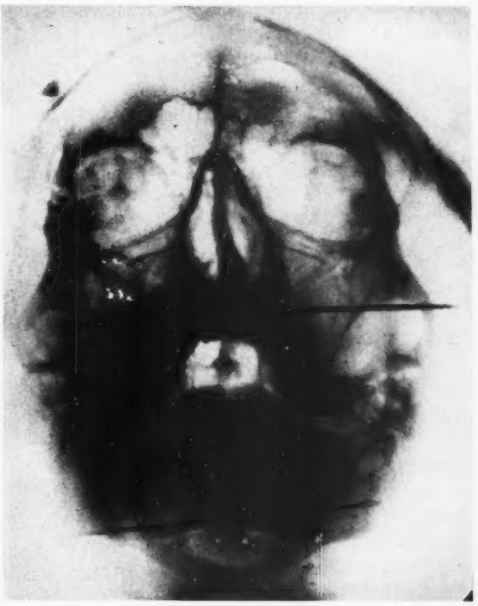

Fig. 3. X-ray film showing internal wires in both upper and lower jaws.

that the internal wire does not fix large fragments grossly out of place, nor tilt them when traversing them.

The canthal regions. The canthal regions are molded by the thumb and finger. If once healed widened and flat, one of the worst problems in plastic surgery arises, that of the displaced inner canthal region. They may be brought up to proper level, but there is great difficulty in getting them back into proper depth.

The lacrimal apparatus may be realigned in this process of early restoration and replacement of the canthal regions, but if these areas are left displaced blockage of the ducts is more apt to occur. Fine adjustment of these many fragments cannot be counted on, but it has been found, in many instances, that early replacement of crushed faces results in functioning lacrimal ducts.

Much of this procedure is literally "doing the reverse of what the accident did." The nose and face are practically inverted on themselves, the nose has to be pulled up out of the

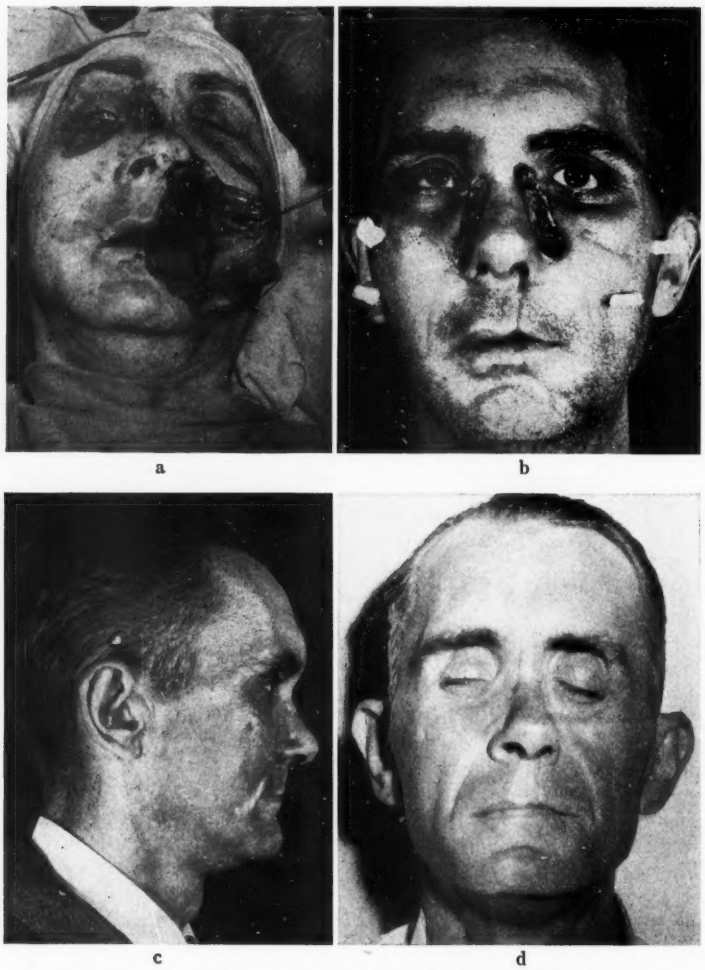

Fig. 4. Complete shattering and widespread avulsion in driver found unconscious at side of road. Operation was performed within 12 hours after clearance of neurosurgical consultants. Bones were shattered into many small fragments and the mass was "mulched" forward and held with cross wires for nose, direct wiring of zygoma, and frontal distention and gauze splinting of antra. Two internal wires across shattered fragments on both sides were used for stabilization. Closure avulsion of soft parts was effected. Patient is shown with internal wires through face. Patient out of hospital with cross wires holding nose. Only one operation was necessary.

face and the face brought forward from its infolding. Débridement should be at a minimum as far as discarding bone or soft tissue is concerned, because this is one area where it may be better to leave in something that might not survive than to throw away something that might live. Primary healing might not result in some instances but the overall benefit would be worth following the rule.

Shortening of the middle third. In bringing forward the face and in elevating the orbital borders the procedures are important in rela-

tion to the frequently described necessity of elevating the upper jaw in transverse facial fractures. Elevation with overhead traction apparatus and through-the-cheek wire from the dental arch are not indicated as frequently or as actively as is sometimes reported, because many transverse facial fractures are already too high and need to be brought down instead of up. The egg shell maxilla and antra may collapse and be jammed upward on themselves instead of coming apart and elongating downward. This condition is seen in traffic accidents in which the jaw strikes the steering wheel or when the lower jaw jams the upper from below. In any event, it is apparent that elevation toward the vertex may be overdone with too much traction, and a permanent deformity may result. One patient has been seen who had to have a denture made that fitted over his own upper teeth because of excessive shortening of the middle third which occurred from overhead traction upward on a transverse fracture that had already collapsed upward.

The whole middle third of the face also has been seen to be carried so far back as to give nasopharyngeal occlusion. This type of injury would not benefit by elevation, but instead the face should be brought forward and downward, if necessary.

Application of the internal wires. Endotracheal anesthesia or a combination of block with light pentothal is used for application of internal wires. They are put in after all possible bone alignment has been obtained. The internal wires are of stainless steel, No. 18-8 of a diameter of .05 to .08 inch, with a spear point for the drilling of the bone, although regular Kirschner wires are usually available and may be relied on. For the upper jaw a hand drill may suffice, but an electric one gives more ease to the problem and to maintaining direction.

If there is marked loss of occlusion there should be anterior arch fixation and interdental wiring in proper occlusion before the internal wire is put in. In the presence of shattering of the arches or splitting of the palate or in edentulous patients, the alignment is done as close to ideal as possible. If interdental wiring is to be done for further fixation or for fracture of the lower jaw, it may appear as though one fractured jaw is used to support another fractured jaw. This is essentially what may be done, the object being to try to insure normal occlusion; this is important when condyles of the lower jaw are broken.

Although occasionally multiple internal wires are needed usually not more than two are necessary. Internal wires in both upper and lower jaws may be indicated as in Figure 3. The ends are protected with adhesive or corks. Although threaded wires with a nipple or nut in place to prevent separation of fragments may be thought necessary, fragments "snub" in place along the plain wires so well that the threaded wire and nipple fixation is rarely needed.

Soft tissue tears are repaired after alignment and immobilization of bone fragments.

Removal of the wires is done within 2 to 6 weeks according to the extent of damage; no anesthesia is necessary. The legends of the illustrations are referred to as part of the text.

Conclusions. This method is not suggested as a cure-all or as replacement of other methods but as a simple, direct, inexpensive addition to the problem of stabilization. When it can be used in place of expensive cumbersome apparatus, the saving may be considerable in equipment, hospitalization, and in the patient's comfort and period of disability.

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THE TREATMENT OF CARDIAC ARREST

An Experimental Study

JEROME HAROLD KAY, M.D., Baltimore, Maryland

CARDIAC arrest is a surgical emergency for which the proper treatment must be instituted immediately. It may occur in one of two forms: (1) ventricular standstill, or (2) ventricular fibrillation. In ventricular standstill the heart is contracting feebly or not at all. In ventricular fibrillation there are inco-ordinate contractions of individual muscle fibers. In both forms the ventricles are ineffective in expelling blood. It is possible to differentiate the two by direct vision or by electrocardiography. The differentiation is extremely important since the treatment of the two conditions is different.

Cardiac arrest may occur during any type of operative procedure on any part of the body with any anesthetic agent. Although it may occur in people with a normal cardiovascular system, it is more likely to occur in patients undergoing operation on the heart, and the frequency of cardiac arrest is increased if the heart is diseased. Cooley reported an incidence of ventricular standstill of 5.5 per cent in 878 patients operated upon for pulmonic stenosis.

Various forms of treatment have been advocated for cardiac arrest. The following investigation was therefore undertaken to try to determine the most satisfactory methods of treating ventricular standstill and fibrillation.

METHODS

Seventy-two male and female mongrel dogs weighing 6 to 15 kilograms were used in these experiments. Cardiac arrest was produced and successfully treated 205 times. In many of the animals cardiac arrest was produced and treated as many as 5 to 10 times during a period of 3 to 4 hours. Toward the end of the experiment the cardiac arrest was more difficult to treat. Forty-eight of the animals were given 16 milligrams of morphine and 0.4 milligram of atropine ½ hour before the experiment. Electrocardiograms were taken or recordings of femoral arterial blood pressures were made with an electromanometer. A constant slow infusion of 5 per cent glucose in water, with 50 milligrams of heparin per liter prevented clotting of the blood in the cannula. Ether anesthesia and artificial respiration were administered by positive pressure through an endotracheal tube with the use of the apparatus described by Hanlon, Johns, and Thomas.

Ventricular standstill was produced by deep anesthetization of the animals with chloroform or ether administered by the open drop method. After the blood pressure had been unobtainable for 3 or more minutes, an endotracheal tube was inserted and positive pressure artificial respiration was instituted. The chest was entered through the left fifth interspace and the pericardium was opened.

The apparatus used to produce and treat ventricular fibrillation consisted of a foot switch, a Variac transformer to regulate the voltage, and two brass electrodes. The electrodes consisted of a brass disc 1 inch in diameter with a brass rod 9 inches in length and ¼ inch in diameter. The handles were insulated with ⅛ inch rubber tubing. The discs were padded with 16-ply gauze sponges and soaked in an isotonic saline solution before each shock.

Ventricular filbrillation was produced by passing a 30 volt-60 cycle alternating current directly through the heart. In 168 of the experiments the ventricles were allowed to fibrillate for 3 or more minutes during which time the heart was massaged. At the end of this time electrical defibrillation, as described in a subsequent paragraph, was attempted. In order to make the ventricular fibrillation as well as the resultant standstill following de-

From The Department of Surgery of The Johns Hopkins University and Hospital. Aided by a grant from the U. S. Public Health Service, National Heart Institute.

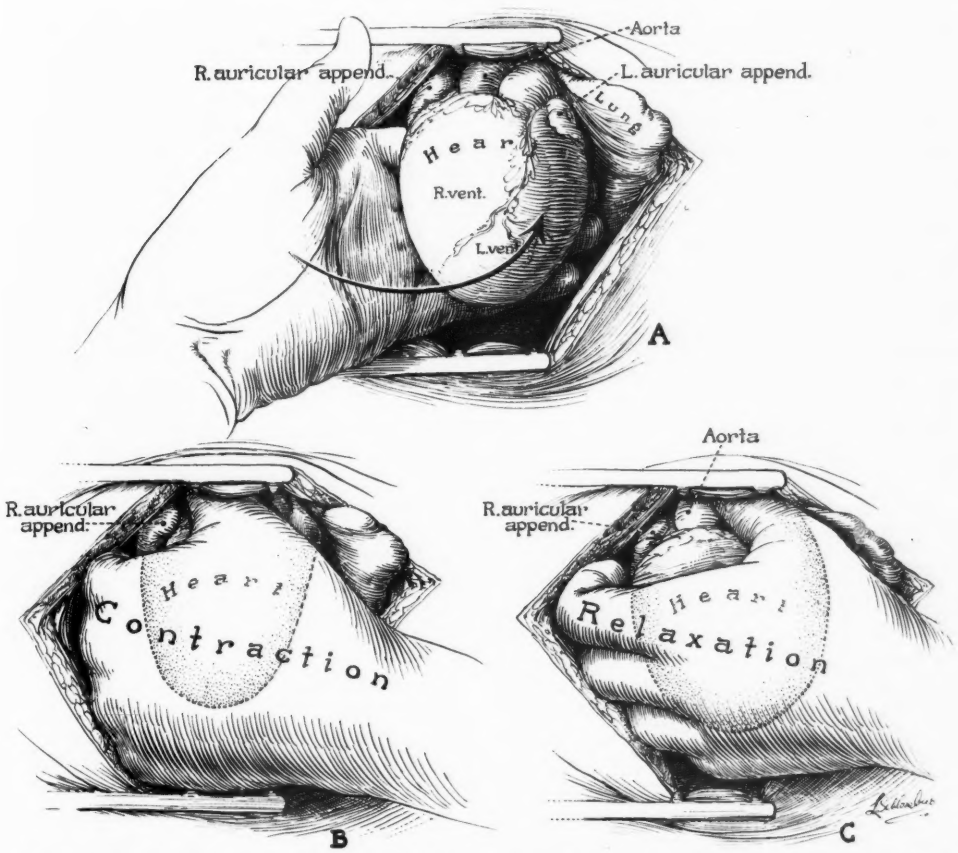

Fig. 1. Cardiac massage. In small hearts cardiac massage is employed as indicated in this drawing; in larger hearts, however, it may be necessary to massage the heart with one hand in front and the other in back of the heart.

fibrillation more difficult to treat, in 25 experiments the heart was allowed to fibrillate 2½ to 7 minutes before cardiac massage was begun and defibrillation was attempted. By making the cardiac arrest more difficult to treat it was possible to carry out more adequate tests with various cardiac stimulants and the one depressant used.

In the treatment of ventricular standstill as well as ventricular fibrillation adequate cardiac massage was found to be extremely important for successful resuscitation. The method of cardiac massage that was most effective was as follows: with the operator on the left side of the operating table and the pericardium open, the left hand was inserted through the left fifth interspace; the fingers were placed on the right side of the heart and the thenar eminence on the left side. The heart was then deliberately and firmly squeezed 35 to 50 times per minute. This rate was rapid enough to maintain adequate circulation and yet did not tire the hand of the operator (Fig. 1). Using this method systolic and diastolic pressures produced by cardiac massage were recorded in 112 cases of ventricular standstill and fibrillation. In 26 per cent of the cases recorded systolic pressures ranged between 40 and 55 millimeters of mercury; in 31 per cent, between 60 and 75 millimeters of mercury; in

43 per cent, between 80 and 160 millimeters of mercury.

If the heart was beating feebly, massage immediately following systole produced pressures 10 to 15 millimeters of mercury higher than if the heart was massaged just prior to systole.

The substances employed were injected into the right auricular or the left ventricular cavity. Injections were made into the left ventricular cavity on more than 150 occasions without once inducing ventricular fibrillation. The left ventricular cavity was found to be the best site since after a few moments of massage the heart usually responded and there was no bleeding from the point of injection during the subsequent massage as usually occurred when the auricle was punctured.

RESULTS

Ventricular standstill. Ventricular standstill was produced by deep anesthetization of 12 animals with open drop chloroform or ether. Ventricular standstill also occurred on 148 occasions following the successful electrical defibrillation of hearts in ventricular fibrillation. Isopropylepinephrine, barium chloride, calcium chloride, and epinephrine hydrochloride were used in the treatment of ventricular standstill.

Of the 12 animals in which ventricular standstill was produced by deep anesthetization with ether or chloroform, 6 responded to cardiac massage alone in from 1 to 3 minutes. The other 6 responded to cardiac massage and a single injection of isopropylepinephrine, calcium chloride, or epinephrine hydrochloride.

The ventricular standstill that occurred 148 times following the successful electrical defibrillation of the heart in ventricular fibrillation was treated by massage, and in 108 cases it was also necessary to inject various cardiac stimulants to restore a normal beat. The results are as follows.

With the various reports of Lands, Nash, McCarthy, Granger, and Dertinger, Nathanson and Miller, and Garb and Chenoweth on the properties of isopropylepinephrine in mind, quantities of this drug[1] ranging from 1 cubic centimeter of a 1:25,000 to 1 cubic centimeter of a 1:500 solution were used in the treatment of ventricular standstill. It was hoped that this would be an effective cardiac stimulant in the treatment of this condition and that it would not cause ventricular fibrillation. Following successful electrical defibrillation the isopropylepinephrine was effective in the treatment of most cases of ventricular standstill that resulted; however, it failed to restore a good beat in many of the hearts that had been used for experimentation for several hours. When the isopropylepinephrine was effective, it caused good contractions immediately.

The results with 2 to 4 cubic centimeters of ½ per cent barium chloride, prepared within an hour or two before being used, were similar to those with isopropylepinephrine. Barium chloride caused good contractions in some cases of ventricular standstill following successful electrical defibrillation of the heart; however, it was not as satisfactory a cardiac stimulant as 2 to 4 cubic centimeters of 10 per cent calcium chloride. In 5 cases when barium chloride failed to restore good contractions, 2 to 4 cubic centimeters of 10 per cent calcium chloride improved the contractions. Barium chloride never produced strong contractions if calcium chloride had failed. Nor did barium chloride improve cardiac contractions immediately after intracardiac injection but only after approximately 2 minutes. Calcium chloride produced its effect immediately.

Calcium chloride was a better cardiac stimulant than isopropylepinephrine or barium chloride. By far the best cardiac stimulant, however, was 0.1 cubic centimeter of 1:1000 epinephrine hydrochloride in 5 cubic centimeters of isotonic saline. It not only was successful when it was the only stimulant used but in every instance when all of the other cardiac stimulants had failed to restore good contractions, 0.1 to 0.2 cubic centimeter of 1:1,000 epinephrine hydrochloride was spectacularly successful.

The quantity of epinephrine hydrochloride used was of considerable importance, for if 0.1 to 0.2 cubic centimeter of 1:1,000 epinephrine hydrochloride was injected the desired cardiac contractions were obtained. However,

[1]The hydrochloride of isopropylepinephrine known as isuprel was used.

following the successful electrical defibrillation of 10 hearts in ventricular fibrillation, 5 to 10 times that dose—or 1 cubic centimeter of 1:1,000 epinephrine hydrochloride—was injected into the left ventricular cavity and 3 of the hearts went into ventricular fibrillation. In comparison with smaller doses of epinephrine hydrochloride this larger dose caused pronounced tachycardia and hypertension.

A mixture of 0.5 cubic centimeter of 1:1,000 epinephrine hydrochloride and 9.5 cubic centimeters of 1 per cent procaine[1] was used in the treatment of ventricular standstill; this mixture appeared to have the stimulating effect of approximately 0.3 or 0.4 cubic centimeter of 1:1,000 epinephrine hydrochloride and therefore also produced pronounced tachycardia and hypertension in comparison with 0.1 or 0.2 cubic centimeter of 1:1,000 epinephrine hydrochloride.

Ventricular fibrillation. In 25 experiments the heart was electrically fibrillated and allowed to fibrillate for 2½ to 7 minutes before the institution of cardiac massage or any other form of therapy. In none of these instances did the fibrillation stop before a lapse of 5 minutes. Four out of 14 hearts (29 per cent) in ventricular fibrillation that lasted from 5 to 7 minutes stopped fibrillating without treatment because the individual muscle fibers were very anoxic. In these 4 cases the heart was dilated, cyanotic, and flabby and there was not the feeblest attempt at cardiac contraction. It was necessary to begin cardiac massage and to inject various cardiac stimulants in order to restore a good beat to all of the hearts that had stopped fibrillating. Therefore, allowing the heart to fibrillate without employing cardiac massage is not an effective method in the treatment of ventricular fibrillation for two reasons: (1) only 29 per cent of the hearts stopped fibrillating if allowed to fibrillate 5 to 7 minutes, and (2) Weinberger, Gibbon, and Gibbon have shown that if a heart is in cardiac arrest for 3 minutes 25 seconds or more without cardiac massage, there will be irreparable damage to the brain.

In 35 experiments the hearts were electrically fibrillated and cardiac massage was immediately instituted. At the end of 2 minutes of massage, procaine in doses ranging from 6 to 90 milligrams per kilogram of weight was injected into the right auricular or the left ventricular cavity. Cardiac massage was continued for another 2 to 8 minutes, and in none of the 35 attempts was there any evidence of improvement in the ventricular fibrillation.

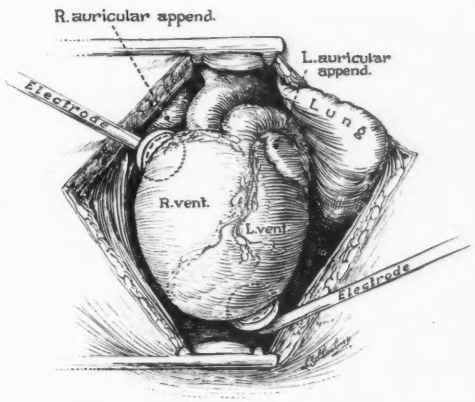

Fig. 2. Position of electrodes for defibrillation. One electrode is placed on the right ventricle in the sulcus between the ventricle and the right auricular appendage; the other electrode is placed on the apex of the heart.

Electrical defibrillation was successful in the treatment of 189 cases of ventricular fibrillation. This procedure was accomplished most frequently by first massaging the heart until it was no longer dilated or cyanotic, this usually requiring 1 or 2 minutes. The electrodes soaked in isotonic saline solution were then placed on the right side of the right ventricle immediately beneath the right auricular appendage and on the left ventricle at the apex of the heart (Fig. 2). A 130 volt 60-cycle alternating current of 1 second or less was passed through the heart and was usually successful in defibrillating it. If the heart was not defibrillated after several attempts, it was massaged for another minute or two and a series of shocks, each of 130 volts and lasting ⅓ second with a ⅓ second interval between the shocks, was passed through the heart. This is serial defibrillation and was first described by Wiggers (31). It was found to be a more effective method of defibrillating the heart than the use of single shocks. If a series of 6 to 8 shocks

[1]In this study a procaine amide hydrochloride known as pronestyl hydrochloride was used.

was unsuccessful on the first attempt, the heart was massaged for another minute and serial defibrillation again attempted.

In 29 animals ventricular fibrillation was electrically produced and the hearts were allowed to fibrillate 3 to 62 minutes before they were electrically defibrillated. During the period of fibrillation the circulation was maintained by cardiac massage at the rate of 35 to 50 times per minute. All of the hearts were successfully defibrillated electrically with single shocks or serial defibrillation, and in this series it was not necessary to use procaine as an adjunct. At the conclusion of each experiment the wound was closed and the animal returned to his cage. All of the animals recovered without evidence of neurological changes. One animal died of empyema on the fourth postoperative day and another of distemper on the twentieth postoperative day. Twenty-four animals were killed between the third and the twentieth postoperative day. Examination showed small superficial burns extending 1 millimeter in depth on 2 of the hearts at the site where one of the electrodes had been placed. There were several ecchymotic areas 1 millimeter in diameter on the ventricle of one of the other hearts. These were apparently due to massage. None of these injuries appeared to be significant and the other hearts were grossly normal. Three dogs were killed on the thirty-first, thirty-sixth, and forty-third days. In these animals the heart had been allowed to fibrillate for 26, 42, and 62 minutes before defibrillation. Postoperative electrocardiograms were essentially normal, and at autopsy the hearts were seen to be grossly and microscopically normal.

In 43 other animals ventricular fibrillation was electrically produced 160 times and successfully treated by electrical defibrillation without a failure. In these animals ventricular fibrillation had been present for at least 3 minutes, and on 135 occasions the heart was massaged during the entire period of fibrillation. In 25 of these experiments the heart was allowed to fibrillate for 2½ to 7 minutes before cardiac massage was begun. In these cases the hearts were massaged for 1 or 2 minutes before electrical defibrillation was attempted. One hundred forty-seven cases of ventricular fibrillation responded to single shocks or to serial defibrillation. In 1 instance it was necessary to use procaine in association with electrical defibrillation. This was the only case in the entire series of experiments in which it was necessary to use procaine in order to defibrillate the heart electrically. In 12 of the experiments 10 cubic centimeters of 1 per cent procaine were used along with electrical defibrillation. Procaine appeared to be of little assistance in electrical defibrillation and made the ventricular standstill following successful electrical defibrillation more difficult to treat.

DISCUSSION

Cardiac massage is extremely important in the treatment of cardiac arrest, for without it most cases of cardiac arrest would terminate fatally. Cardiac massage is most effective when employed through the open pericardium. Beck and Mautz (5) and Barber and Madden recommend massaging the heart 40 to 50 times per minute. Wiggers (30) was able to maintain aortic pressures between 60 and 85 millimeters of mercury by massaging the heart 40 times per minute. Johnson and Kirby measured the blood flow of the carotid or the femoral artery with the use of a bubble meter while massaging the heart at various rates ranging from 30 to 120 times per minute. They concluded that the optimal rate of cardiac massage is the most rapid rate at which the heart can be compressed, at least up to 120 times per minute. They stated, however, that a rate of 120 per minute could not be continued for more than a few minutes by one person because of cramping in the forearm. They felt, therefore, that a substitute should be provided for the operator in order to maintain a rapid rate. From my experimental results described in this paper it seems adequate to massage the heart at the rate of 50 times per minute. In 14 animals cardiac arrest was present for 3½ to 62 minutes. The circulation during this period was maintained by cardiac massage at the rate of 35 to 50 times per minute. At the conclusion of the experiment the heart beat was restored and the chest wall was closed. None of these animals showed postoperative neurological changes. This rate of cardiac massage would therefore appear to be

adequate, for Weinberger, Gibbon, and Gibbon have shown that if untreated cardiac arrest is present for 3 minutes and 25 seconds or longer there will be permanent alterations in behavior and psychic function in the animal. If the arrest is present for 8 minutes and 45 seconds, life can be restored for only a few hours. This slower rate of massage would appear to be more practical than a more rapid one, since in these experiments one operator was able to continue with cardiac massage for periods as long as 62 minutes without fatigue.

Ventricular standstill. In the treatment of ventricular standstill it is important to massage the heart for 1 to 2 minutes before injecting any cardiac stimulant. Many cases of ventricular standstill responded to 1 to 2 minutes of cardiac massage alone. Those hearts that did not respond to cardiac massage alone began to beat well after the injection of one of several cardiac stimulants. If the cardiac stimulant was injected without previous massaging of the heart, ventricular fibrillation frequently ensued from the substance injected or from the needle puncture through the ventricular wall. Hyman and Barber and Madden believe that to obviate the danger of producing ventricular fibrillation the right auricle should be the site of injection. In the experiments recorded here, in over 150 injections into the left ventricular cavity preceded by cardiac massage for 1 to 2 minutes, not 1 case of ventricular fibrillation was produced. It must be emphasized, however, that unless the heart is massaged for 1 to 2 minutes before puncturing the ventricular cavity, ventricular fibrillation may follow. Furthermore, the left ventricular cavity was the preferred site for the injection since after a few moments of massage, the substance was in the coronary vessels and in the myocardial bed. Massage prior to the injection increased the possibility of restoring a normal beat with the injection and also prevented the occurrence of ventricular fibrillation. It was important to massage the heart after as well as before the injection in order to circulate the substance into the myocardium.

Nathanson and Miller thought isopropylepinephrine might be of practical value in the treatment of sudden cardiac standstill. In the experiments reported in this paper it was frequently successful in hearts that did not respond to massage alone; however, it was not a satisfactory stimulant in hearts that had been used for experimentation for several hours. Fauteux on the basis of his experiments recommends the use of 2 cubic centimeters of freshly prepared ½ per cent barium chloride for the treatment of ventricular standstill. In this laboratory, however, barium chloride, prepared within an hour or two of its use, was no more effective than isopropylepinephrine. Two to 4 cubic centimeters of 10 per cent calcium chloride was a better cardiac stimulant than isopropylepinephrine or barium chloride and frequently restored a normal beat after the other two had failed.

In the dog epinephrine hydrochloride was the most effective cardiac stimulant and restored good contractions when the other stimulants had failed. In man, however, Doctor Blalock and I have presented evidence that calcium chloride may be as effective as epinephrine hydrochloride in the treatment of ventricular standstill. Beck (6) recommends 0.5 cubic centimeter of 1:1,000 epinephrine hydrochloride diluted in 5 cubic centimeters of sodium chloride solution. Beecher and Linton state that it is doubtful whether more than 0.2 or 0.3 cubic centimeter of 1:1,000 epinephrine hydrochloride should be used in the treatment of ventricular standstill. In the present experiments with this condition a single injection of 0.1 cubic centimeter of 1:1,000 epinephrine hydrochloride in 5 cubic centimeters of normal saline solution almost always restored a normal beat; if the first injection failed, a second injection of the same strength was usually effective. It was not often necessary to inject 0.2 cubic centimeter of 1:1,000 epinephrine hydrochloride. If quantities as large as 1 cubic centimeter of 1:1,000 epinephrine were used following successful electrical defibrillation of the heart, 30 per cent of the hearts went into ventricular fibrillation. It would seem to be safer to use a small dose of epinephrine hydrochloride and to repeat the dose and increase it as necessary rather than to inject a large dose immediately and thereby run the risk of producing ventricular fibrillation.

Lahey and Ruzicka inject a mixture of 0.5 cubic centimeter of 1:1,000 epinephrine hydrochloride and 9.5 cubic centimeters of 1 per cent procaine in a single injection when the diagnosis of cardiac arrest is made. Anderson, Schock, and Faxon also use this same mixture in the treatment of cardiac arrest as they state that one can rarely be sure whether cardiac standstill or ventricular fibrillation is present. Experimentally this mixture has a stimulating effect which appears to be comparable to that of 0.3 or 0.4 cubic centimeter of 1:1,000 epinephrine hydrochloride. In the treatment of ventricular standstill it is safer to use 0.1 or 0.2 cubic centimeter of 1:1,000 epinephrine hydrochloride instead of this mixture. The mixture should not be used in the treatment of ventricular fibrillation because the use of cardiac stimulants is usually not indicated in the treatment of this condition. It is usually not difficult to differentiate between ventricular fibrillation and ventricular standstill; if there is difficulty in determining the form of cardiac arrest present, cardiac massage alone for 1 to 2 minutes will restore a good beat in many of the cases of ventricular standstill and will accentuate the ventricular fibrillation by restoring some of the tone to the anoxic fibrillating muscle and differentiation, therefore, will usually be possible.

Ventricular fibrillation. Chemical defibrillation of the heart was experimentally employed by d'Halluin, Hooker (15), and Wiggers (29). They successfully defibrillated the heart by injecting potassium chloride intravenously, intra-arterially, or intracordially. This produced ventricular standstill and it was necessary to inject a stimulant to restore cardiac contractions. For the cardiac stimulant they injected calcium chloride, epinephrine hydrochloride, or both until the desired improvement was obtained. Chemical defibrillation was not a satisfactory method for the treatment of ventricular fibrillation and failures occurred frequently. If it was successful, 6 minutes were frequently required for the potassium to have its effect and the heart could not be massaged during this period. It was impossible to determine the exact quantity of potassium needed to stop the ventricular fibrillation. The amount of calcium injected to counteract the effect of potassium and thereby restore a normal beat was also determined empirically. If the quantity of potassium injected was too small, the fibrillation persisted. If too much potassium was injected, the resulting standstill was difficult to treat. Too large an amount of calcium would cause the ventricles to revert to fibrillation. This method was therefore abandoned by these investigators.

Burstein, Marangoni, DeGraff and Rovenstine reported that procaine was efficient in the treatment of 66 per cent of their animals in which ventricular fibrillation had developed. Stutzman, Allen, and Orth produced unequivocal ventricular fibrillation and treated it with intravenous or intracardiac injections of procaine. Not a single instance of fibrillation was altered by this treatment. They believed that in many of Burstein's animals the heart was not fibrillating and that similar cases of their series reverted to normal rhythm without any treatment. Smith and Ferguson (25), using intracordial injections of procaine, were unable to restore a normal rhythm to fibrillating ventricles. Stearns, Maison, and Stutzman (26) injected procaine into hearts in ventricular fibrillation, and after 30 to 45 minutes of continuous cardiac massage asystole occurred spontaneously in 50 per cent of their animals. However, despite the administration of a sympathomimetic drug only 20 per cent of their animals were able to maintain their blood pressure without massage for any length of time. There were no survivals. In the 35 attempts reported in the present paper it was impossible to defibrillate a single heart by injecting procaine and continuing massage for 2 to 8 minutes.

Lampson, Schaeffer, and Lincoln stated that there are two practical methods of interrupting ventricular fibrillation: namely, the use of electric shock and the administration of procaine hydrochloride into the blood stream. They also stated that the two methods may be used separately or as adjuncts to each other. There appears, however, to be only one practical and consistently successful method of defibrillating the heart and that is by electrical means. This method was first described in 1899 by Prevost and Battelli. Subsequently

Hooker, Kouwenhoven, and Langworthy, as well as Wiggers (30) and Beck and his associates (3, 4, 5, 6, 7), reported their success with the method. The most satisfactory method consists of cardiac massage until the heart is no longer dilated or cyanotic followed by the application of single shocks or a series of shocks. In ventricular fibrillation in man Beck (4) recommends massage, the application of 5 to 10 cubic centimeters of 1 per cent procaine hydrochloride to the surface of the heart and also injected into the blood stream, and the application of electrical shock to the ventricles. Wiggers (31) stated that procaine may have an adjuvant action in electrical defibrillation of the heart, but before this depressant was used more substantial evidence of its effectiveness was needed than was furnished by the methods so far devised. Beck and Mautz (5) also noticed the depressant effect of procaine and advised the injection of various cardiac stimulants to counteract this effect. The experimental results here recorded tend to indicate that procaine should not be used unless serial defibrillation has failed after many attempts. Although the procaine appeared to be of slight assistance in electrical defibrillation of the heart, the ventricular standstill that may result following successful electrical defibrillation was more difficult to treat if 10 cubic centimeters of 1 per cent procaine had been used, and in most experiments this disadvantage appeared to outweigh the advantage in the use of procaine.

SUMMARY

1. Ventricular standstill and fibrillation were produced 205 times in 72 dogs and various forms of treatment were employed and evaluated.

2. Adequate cardiac massage was found to be one of the most important steps in treating ventricular standstill and fibrillation

3. Ventricular standstill produced by an overdose of ether or chloroform as well as ventricular standstill following the successful electrical defibrillation of hearts in ventricular fibrillation was successfully treated with cardiac massage alone or cardiac massage in conjunction with the injection of various cardiac stimulants.

4. Isopropylepinephrine and barium chloride restored a normal beat to many of the hearts in ventricular standstill. Calcium chloride was a better cardiac stimulant than these two, but epinephrine hydrochloride was the best cardiac stimulant.

5. The injection of procaine is not a satisfactory method of treating ventricular fibrillation even when accompanied by cardiac massage.

6. In 189 experiments cardiac massage for 1 to 2 minutes associated with electrical defibrillation was successful in defibrillating all of the hearts in ventricular fibrillation.

7. On only 1 occasion was it necessary to use procaine as an adjunct to electrical defibrillation.

8. In 29 animals the heart was allowed to fibrillate for periods varying from 3 minutes to 62 minutes. The heart was massaged during the entire time and at the end of the allotted time the heart was electrically defibrillated and all of the animals recovered without evidence of neurological changes.

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MECHANISM OF ELECTROLYTE IMBALANCE FOLLOWING URETEROSIGMOID TRANSPLANTATION

JACK LAPIDES, M.D., Ann Arbor, Michigan

FOLLOWING the introduction of Coffey's techniques for ureterointestinal anastomosis, transplantation of the ureters to the bowel became a popular and practical operation. It was soon noted that a large number of the patients subjected to the operation developed intermittent episodes of anorexia, nausea, fatigue, fever, and occasionally nitrogen retention at varying periods following operation. With the advent of excretory pyelography it was discovered that dilatation of the ureters and kidney pelvis was almost a universal sequel to this operation; and the morbidity of the patients was attributed to the complications of obstruction at the site of anastomosis.

The advent of chemotherapy and antibiotics brought about improved results following the employment of the Coffey technique and permitted the development of numerous new techniques of anastomosis, with the result that a lessened incidence of postoperative dilatations has occurred. But there has not been a corresponding decline in the incidence of postoperative morbidity. Further investigations (16) into this problem have demonstrated the morbidity to be associated with an electrolyte imbalance manifested by hyperchloremia and acidosis.

Recent reports (16, 18, 35) conclude that the electrolyte disturbance is primarily due to absorption of urinary constituents from the colon. But the theory of intestinal absorption fails to account for several apparent discrepancies. If intestinal absorption alone is the etiological factor, then one would expect electrolyte imbalance in all patients soon after transplantation of the ureters. However, a significant number do not demonstrate electrolyte imbalance at all, and many that do evidence hyperchloremia with acidosis do not develop the abnormality until months or even years after operation. Another discrepancy concerns the economy of urea. If intestinal absorption were the only factor involved in the imbalance in question, then an elevated blood urea nitrogen level should be a constant finding since urea is the major solute of urine, and urea is an extremely diffusible substance. Yet many patients do not have elevated blood urea nitrogen after transplantation of the ureters; indeed many of the patients who display hyperchloremia with acidosis are found to have normal urea nitrogen blood levels.

A mechanism which accounts for all of these phenomena has been demonstrated by the investigations described herein. The data reveal that the chemical imbalance in question is caused by a dual mechanism; the first factor, *renal tubular damage*, is believed to be the determinative factor for without it electrolyte imbalance has not been observed; the other factor, *intestinal absorption of urinary constituents*, while important, plays only a secondary role.

The investigation was conducted in several parts. In the first portion observations involving blood electrolyte studies, excretory pyelography, and postmortem examination were made on patients and dogs who had undergone bilateral ureterosigmoid transplantation; electrolyte studies were obtained also in patients not subjected to ureterointestinal anastomosis but who suffered from bilateral pyelonephritis, hydronephrosis, or both. Additional observations were made on the effects of rectal instillation of urine on the electrolyte balance of 3 patients with normal and 3 patients with abnormal renal function.

SECTION I

METHODS

Blood studies. Blood studies including *p*H, total plasma bicarbonate, plasma chloride,

From the Departments of Surgery, University of Michigan Medical School, Ann Arbor, Michigan and Wayne County General Hospital, Eloise, Michigan.

This investigation was supported in part by the George L. McKesson Fund for Urological Research and by a Public Health Service Postdoctorate Research Fellowship from the National Cancer Institute.

TABLE I.—ELECTROLYTE BALANCE IN 6 PATIENTS

Patient, age, sex	Month, p.o. transplantation and technique	pH	HCO_3— mEq./L.	Cl— mEq./L.	Prot. mEq./L.	Inorganic P mgm.%	Na+ mEq./L.	K+ mEq./L.	Total base mEq./L	B.U.N. mgm.%	N.P.N. mgm.%	Diagnosis
C.J. 55 ♂	3(N)	7.4	23.3	102	16.7	4.0			159	12.3		Bladder neoplasm
I.Z. 48 ♀	10(N)	7.34	23.7	98	19.1	4.1	138	4.8	155		31	Interstitial cystitis
S.H. 62 ♂	14(N)	7.34	21.3	105	17.5	4.0			155	24		Bladder neoplasm
L.S. 7 ♂	72(C)	7.34	23.0	99	15.8	5.8			155	20.7		Bladder exstrophy
F.G. 5 ♂	60(C)	7.45	22.9	105	17.5	6.6	143	4.69	160	20.7		Bladder exstrophy
R.S. 49 ♂	48(C)	7.35	20.2	105	15.8					11.7		Bladder neoplasm

plasma protein, plasma inorganic phosphate and total base were determined on venous blood in accord with the methods described by Reardon and co-workers. Serum sodium and potassium values were obtained by the method of flame photometry (8) and blood urea nitrogen by the method of Archibald. The above determinations were obtained on: (a) patients who had undergone bilateral ureterosigmoid transplantation for such diseases as bladder neoplasm, exstrophy of the bladder, severe interstitial cystitis, and urinary incontinence; (b) dogs subjected to bilateral ureterosigmoid transplantation; and (c) patients with such renal diseases as bilateral pyelonephritis, hydronephrosis, or both.

RESULTS

Electrolyte studies. Analysis of the electrolyte investigations carried out on 22 patients revealed several patterns under which the patients could be classified.

Six patients were found to be in electrolyte balance throughout their follow-up study. The electrolyte profiles obtained most recently are depicted in Table I. These patients feel perfectly well and have never demonstrated signs or symptoms of pyelonephritis. The Coffey technique of transplantation was used in 3 patients while the Nesbit elliptical method was employed on the remainder.

Sixteen patients demonstrated electrolyte imbalance at one time or another at varying periods following transplantation. Thirteen of the 16 patients evidenced hyperchloremia; 11 of these had a decreased carbon dioxide combining power. In Table II are shown the blood levels obtained on these 13 patients. It will be observed that 6 patients demonstrate elevated blood phosphorus levels and 6 patients show abnormal blood urea nitrogen values. All of the 13 indicate essentially normal total base. Most of the patients listed in Table II have had intermittent recurrent attacks of flank pain associated with fever, malaise, nausea, and vomiting. It is interesting to note that the patient (T.W. 51 in Table II) who demonstrated the most severe hyperchloremia had borderline renal function prior to operation; urea clearance was approximately 24 per cent preoperatively. The patient was a known hypertensive. Table III demonstrates his electrolyte profile over a period of several months.

Two patients exhibited a hypochloremia associated with a normal carbon dioxide combining power and a decreased total base for several months after operation. Both patients were feeding problems and on wet colostomies (having had complete removal of their pelvic viscera). Their blood chemistry studies are shown in Table IV.

One patient (A.R.) demonstrated a decreased carbon dioxide combining power associated with normal blood urea nitrogen and chloride values. At a later date the patient's carbon dioxide combining power returned to normal. He eventually died from metastatic neoplastic involvement of the body and was autopsied.

TABLE II.—HYPERCHLOREMIA IN 13 PATIENTS

Patient, age, sex	Months p.o. transplantation	Diagnosis	pH	HCO_3− mEq./L.	Cl− mEq./L.	Protein mEq./L.	Inorganic P mgm.%	Na+ mEq./L.	K+ mEq./L.	Total base mEq./L.	B.U.N. mgm.%	N.P.N. mgm.%
M.K. 50 ♂	17	Bladder neoplasm	7.31	20.3	113	17.5	4.9	139.3	4.5	157	18	
T.W. 51 ♂	24	Bladder neoplasm	7.3	16.1	109	18.3	3.7	142	7.1	156	84	
L.W. 36 ♀	14	Urinary incontinence	7.36	18.9	107	17.5	2.6			152	14.2	
E.D. 62 ♂	32	Bladder neoplasm	7.26	17.0	107	18.3	6.0	140	5.3	152	62	
C.J. 60 ♀	18	Interstitial cystitis	7.34	17.0	112	15.8	4.5			156	14.1	
S.C. 45 ♀	6	Interstitial cystitis		15.0	112		3.5	143				33
W.P. 50 ♂	14	Ca. rectum with metastases to bladder	7.27	5.0	110	20				152		
J.D. 3 ♂	36	Exstrophy bladder	7.35	17.6	113	17.5	6.0			153	27.2	
G.G. 57 ♂	8	Bladder neoplasm	7.24	14.6	113	19.9	4.6			154	42	
M.M. 2 ♀	12	Exstrophy bladder	7.3	14.6	113	17.7	6.7	138.5	5.0	151	27.4	
C.M. 3 ♀	29	Exstrophy bladder		14	113	18.3	7.1			153	63	
E.W. 65 ♂	18	Bladder ca.	7.42	27.4	112	16.7	5.7	138	4.6	159	14.4	
E.N. 58 ♂	7	Bladder ca.	7.48	23.9	108	15.8	5.2			157	19	

Examination of the serum sodium and potassium levels listed in Tables I and II discloses that practically all of them are within normal limits with the exception of patient T.W. in Table II who demonstrated an elevated serum potassium. One patient (L.K.), not shown in any of the tables, entered the hospital with a serum potassium of 2.56 milliequivalents. He developed the hypopotassemia after a week of anorexia and vomiting due to intestinal obstruction.

The electrolyte studies obtained in 4 dogs with ureterosigmoid transplants revealed findings similar to those observed in the human subjects.

Table V shows the electrolyte studies conducted on dog 1; these abnormalities are similar to those of dogs 2 and 3 and of patients in Table II.

Dog 4 immediately postoperatively showed electrolyte changes similar to those found in dogs 1, 2, and 3. However, about 4 weeks following operation, the dog developed fever, anorexia, and vomiting. The dog progressively became worse and died 8 weeks after ureterosigmoid transplantation. Table VI indicates the gradual decrease in carbon dioxide combining power, plasma chlorides, serum sodium, potassium and total base associated with rising blood urea nitrogen and serum protein.

Acidosis with hyperchloremia has been observed in some patients with bilateral pyelonephritis and hydronephrosis, who had not been subjected to bilateral ureterosigmoid transplantation. Some of these patients with their diagnoses and blood chemistry studies are shown in Table VII.

Pyelographic studies. Intravenous pyelograms were obtained preoperatively and 7 to 9 days postoperatively on most of the patients studied. In addition follow-up excretory pyelograms were obtained at 6 to 12 month intervals on the patients who had ureteral transplantation more than 2 years ago and at more frequent intervals on those patients who have been operated upon within the past 2 years.

Analysis of the excretory pyelograms revealed that only 23 per cent of the patients

TABLE III.—ELECTROLYTE PROFILE OF PATIENT T.W.

Date	pH	HCO_3— mEq./L.	Cl— mEq./L.	Protein mEq./L.	Inorganic P mgm.%	Total base mEq./L.	B.U.N. mgm.%
7-15-49		13.4	117	18	4.6	155	48
10-25-49	7.18	12.6	111	19		155	87
11- 3-49	7.3	16.7	117	17.1	7.1	156.5	68.4
12-13-49	7.23	17.2	110	18.3	3.5	153	72
2-27-50	7.24	18.9	110	21.6	7.2	161	72
3-27-50	7.24	16.3	118	18.8	5.3	159	69
4-24-50		19.0	112	19.2	4.9	157	63

maintained normal pyelograms throughout their entire study; these patients with normal pyelograms also demonstrated electrolyte balance. One patient with normal blood chemistry studies and a unilateral hydronephrosis preoperatively evidenced no change either pyelographically or in electrolyte pattern during his follow-up investigations.

Seventy-seven per cent of the patients showed abnormal pyelograms at one time or another during their postoperative period. The abnormalities were either hydronephrosis or nonvisualization of the collecting systems. Eleven patients were followed with excretory pyelography at approximately 3 month intervals. Only 2 of the 11 patients revealed abnormal pyelograms immediately after operation which persisted during their check-up period. The remaining 9 patients had normal pyelograms 1 month following bilateral ureterosigmoid transplantation but then developed abnormal pyelograms at a later date in their postoperative period. The pyelographic disturbances were often of a temporary character, usually preceded by a history of recurrent intermittent attacks of flank pain and fever and frequently associated with hyperchloremia and acidosis. Cessation of the incidents of clinical pyelonephritis, ureteritis, and hydronephrosis for a period of several months would be followed by a return of the pyelographic and electrolyte studies to normal. Figure 1 depicts a case of intermittent pyelographic and electrolyte disturbance occurring in a female, aged 60 years, who underwent bilateral ureterosigmoid transplantation for alleviation of a severe interstitial cystitis.

TABLE IV.—BLOOD CHEMISTRY STUDIES IN 2 PATIENTS

Patient sex	pH	HCO_3— mEq./L.	Cl— mEq./L.	Protein mEq./L.	Inorganic P mgm.%	Total base mEq./L.	B.U.N. mgm.%
L.W. ♀	7.5	25.8	91	17.5	7.5	144	8.5
E.M. ♂	7.47	24.8	95	16.7	5.5	146	10.8

TABLE V.—ELECTROLYTE STUDIES IN DOG 1

Weeks p. o.	pH	HCO_3— mEq./L.	Cl— mEq./L.	Protein mEq./L.	Inorganic P mgm.%	Total base mEq./L.	B.U.N. mgm.%
1	7.26	18.1	116	14.4		159	29
2	7.26	19.9	115	14.4		164	32
3	7.35	18.7	95	17.3		155	18.3
4	7.18	20.2	115	15.3	6	162	15
7	7.26	18.9	121	18	7.4	161	36.7
11	7.20	16.7	117	16.6	8.1	162.5	28
19	7.39	20.6	111	18.2	6.0	157.5	33
22	7.18	15.8	115	14.9	7.6	163	18.9

Figure 1a reveals the preoperative pyelogram; blood chemistry studies were normal at this time. Pyelograms obtained 10 days after operation were essentially normal as were the electrolytes. Several months later the patient returned for a check-up examination and gave a history of having had several episodes of fever and bilateral flank pain. Pyelograms taken at this time (Fig. 1b) revealed a moderate bilateral hydronephrosis. However, no change had occurred in the electrolyte profile. The patient was discharged and returned 3 months later for another examination. She stated that she had been asymptomatic in the interim. Pyelograms (Fig. 1c) were normal as were the electrolytes. Approximately 1 year following operation the patient again returned for follow-up studies and on this visit revealed that she had suffered several episodes of flank pain and fever. Pyelograms (Fig. 1d) again revealed bilateral hydronephrosis and, in addition, blood chemistries for the first time demonstrated hyperchloremia with acidosis (plasma chlorides 112 mEq., plasma bicarbonate 17 mEq., blood urea nitrogen 14.1 mgm. per cent). Six months later pyelograms (Fig. 1e) were found to be essentially normal as were the blood chemistry studies.

TABLE VI.—ELECTROLYTE STUDIES IN DOG 4

Weeks p.o.	pH	HCO_3- mEq./L.	Cl− mEq./L.	Protein mEq./L.	Inorganic P mgm.%	Total base mEq./L.	B.U.N. mgm.%	K+ mEq./L.	Na+ mEq./L.
2	7.30	21.1	105	14	7.5	158	22.7		
3	7.31	25.1	111	16	6.5	159	27.6		
4	7.27	11.7	106	19.8	5.7	154.5	43		
8	7.24	11.6	92	20	7.2	142	60	3.3	125

Examples of delayed development of pyelographic abnormalities associated with electrolyte imbalance are illustrated in Figures 2 and 3. The pyelograms shown in Figure 2 were obtained on a 36 year old female who underwent bilateral ureterosigmoid anastomosis for urinary incontinence. Figure 2a is the preoperative pyelogram; Figures 2b, 2c, 2d, and 2e are respectively the 6, 10, 30, and 74 week postoperative pyelograms. It will be observed that the roentgenograms are all essentially normal except for the 74 week postoperative film (Fig. 2e) which demonstrates moderate bilateral hydronephrosis. Of importance is the fact that electrolyte profiles remained normal until the check-up visit at 74 weeks. Blood studies at that time disclosed the following findings: plasma chlorides 114 milliequivalents, plasma bicarbonate 16.6 milliequivalents, and blood nonprotein nitrogen 23 milligrams per cent. The clinical history indicated that the patient had endured numerous intermittent episodes of pyelonephritis during her entire postoperative period.

In Figure 3a is depicted the 9 day postoperative pyelogram of a 57 year old male who experienced cystectomy and bilateral ureterosigmoid transplantation for bladder neoplasm. Figure 3b was taken 4 weeks, Figure 3c, 11 weeks, and Figure 3d, 54 weeks after operation. Again all pyelograms were normal except for the 54 week postoperative film. Blood chemistry studies were not abnormal until the 54 week check-up when the plasma chlorides were found to be 113 milliequivalents, plasma bicarbonate 14.6 milliequivalents, and blood urea nitrogen 42 milligrams per cent. This patient also had a history of intermittent episodes of flank pain and fever.

Postmortem examination of patients and dogs. Autopsies were carried out on 2 patients. Both examinations revealed extensive metastases originating from bladder neoplasms and more important, bilateral chronic pyelonephritis. One patient demonstrated gross fecal material in the renal pelves bilaterally.

Dog 4 (Table VI) at autopsy was found to have bilateral severe ascending pyelonephritis. Dogs 1, 2, and 3 all demonstrated moderately advanced bilateral chronic pyelonephritis.

The renal pelves of 1 dog contained fecal material at autopsy.

DISCUSSION

From the data accumulated it is apparent that there is a very close relationship between electrolyte imbalance and disturbed renal function and structure as evidenced by clinical studies and pyelographic as well as postmortem examination of the kidneys.

It is not unreasonable for some workers (16, 18, 35) to have attributed the electrolyte imbalance to the absorption of urinary constituents by the large intestine for it has been

TABLE VII.—BLOOD CHEMISTRY STUDIES IN PATIENTS WITH BILATERAL PYELONEPHRITIS AND HYDRONEPHROSIS

Patient, sex	Diagnosis	pH	HCO_3- mEq./L.	Cl− mEq./L.	Protein mEq./L.	Inorganic P mgm.%	Total base mEq./L.	B.U.N. mgm.%	N.P.N. mgm.%
C.D. ♂	Far advanced pyelonephritis and hydronephrosis	7.25	10.9	107	16.7	13.0	158	100+	
B.D. ♂	Chronic urinary retention with chronic pyelonephritis		14.0	117					218
L.B. ♂	Bilateral hydronephrosis and chronic pyelonephritis		15.3	117					93

demonstrated by numerous workers (6, 12, 13, 17, 19, 22, 33, 36, 38) that the large intestine is capable of absorbing water, sodium, chloride, calcium, glucose, arsenic, atropine, and methylene blue. However, the proponents of the "intestinal absorption theory" do not offer satisfactory explanations for the complete absence of electrolyte imbalance in about 25 per cent of the patients or for the relatively delayed development of hyperchloremia with acidosis in a good proportion of the patients. No one has published evidence to indicate that the intestinal epithelium undergoes metaplasia as a result of the prolonged presence of urine in the colon thereby changing the absorptive mechanism of the large intestine.

A review of the clinical postoperative course of the patients presented reveals that all of the patients with electrolyte imbalance suffered intermittent episodes of pyelonephritis. Excretory pyelography demonstrated that all of the patients with electrolyte imbalance gave evidence of either hydronephrosis or nonvisualization of the renal collecting system. In some patients the pyelographic abnormality and electrolyte imbalance were relatively transitory while in others they were persistent. It is interesting to note that in the great majority of cases hydronephrosis did not appear until months or even years after operation, suggesting that its development is independent of the operative procedure in most of the instances and probably due to recurrent infection at the ureterointestinal meatus (20). The high incidence of pyelographic abnormalities in the subjects of this experimental study is in accord with the findings of Pool and Cook who performed excretory urograms in 43 cases of bilateral ureterosigmoid transplants 6 months after operation and found only 5 with normal urographic outlines; the remaining 38 patients exhibited urographic deformity of varying degrees.

Examination of patients and experimental animals who came to autopsy revealed bilateral pyelonephritis of varying degrees in all the subjects. These observations are similar to those of Graves and Buddington who found chronic pyelonephritis in every patient with bilateral ureterointestinal anastomoses who came to autopsy with the exception of 1.

It is thus evident that renal disease and electrolyte imbalance are interrelated in ureterointestinal anastomosis. Some workers find it difficult to associate hyperchloremic acidosis with renal impairment in the face of a normal blood urea nitrogen or nonprotein nitrogen. A review of the literature will reveal that hyperchloremic acidosis with normal blood urea nitrogen can occur in individuals with abnormal function of the renal tubule. During the era of sulfanilamide therapy it was observed by several investigators (7, 24, 31, 34) that hyperchloremic acidosis frequently occurred in human patients following use of sulfanilamide. The blood nitrogen levels were normal despite the electrolyte imbalance. Further investigation (14, 23) revealed that sulfanilamide inhibits the enzyme carbonic anhydrase. Pitts and Alexander proposed that carbonic anhydrase inhibition results in dysfunction of the base conservation mechanism of the distal tubules.

Another disease syndrome characterized by Albright (1) as "renal acidosis resulting from tubular-insufficiency-without-glomerular insufficiency" has been observed in children (2, 9, 10, 15, 26, 32) and in adults (5, 21). As in the sulfanilamide cases these patients also manifest hyperchloremia, acidosis, and normal blood urea nitrogen levels. Pathological changes in the tubule with absence of diffuse glomerular changes have been noted in 3 cases coming to necropsy (1, 5, 9). Practically all of the investigators are agreed upon the fact that the electrolyte disturbances are primarily due to aberration in the base conservation mechanism of the renal tubule, especially the distal segment. The exact mechanism leading to lowering of plasma bicarbonate and elevation of plasma chloride in these cases has not been definitely established to date and thus no discussion will be given to this phase of the subject; the reader is referred to the bibliography (1, 2, 5, 9, 10, 15, 21, 26, 27, 32) for theories concerning the mechanism of development of hyperchloremic acidosis.

Having demonstrated that electrolyte imbalance can occur in renal disease without disturbance of the blood urea nitrogen, it would now be appropriate to apply this knowledge to the renal malady that occurs so com-

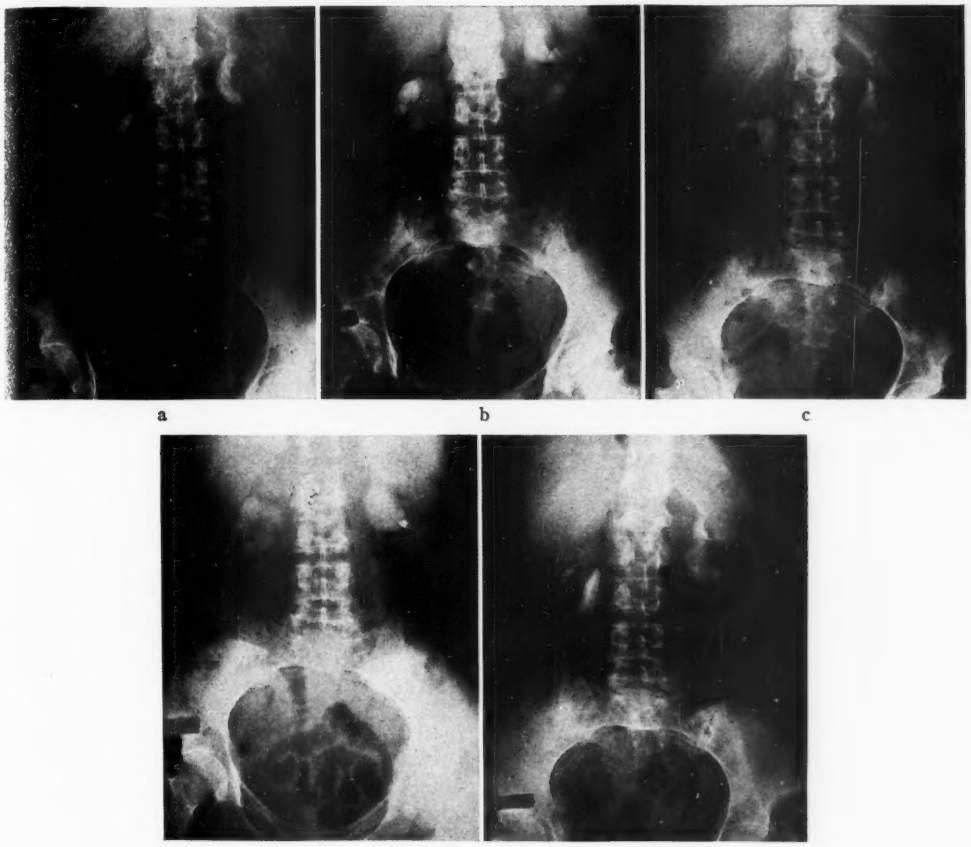

Fig. 1.

monly in ureterosigmoid transplantation, namely pyelonephritis. Pyelonephritis has been described (3) as an interstitial inflammation of the renal pelvis and parenchyma of the kidney. The infection, produced most commonly by the bacteria of the coli-aerogenes group, may either be hematogenous in origin or ascending through the ureteral lumen or by way of the periureteral lymphatics. It is obvious that in ureterointestinal anastomoses the mode of origin is primarily ascending. The pyelographic evidence presented in this paper demonstrated quite clearly the high incidence of hydronephrosis which in itself predisposes to pyelonephritis. Urograms made by injecting radio-opaque material into the rectum have demonstrated ureteral reflex in a number of patients. In addition necropsy has revealed gross fecal material in the renal pelves in 1 patient and in 1 dog.

Initially pyelonephritis involves the collecting ducts and renal tubules; eventually the glomeruli become involved (29, 37). Raaschow has demonstrated by means of clearance tests that tubular injury is predominant in pyelonephritis. The electrolyte studies obtained in our patients with far advanced pyelonephritis but without transplants (Table VII) indicate that hyperchloremia with acidosis can occur in patients with pyelonephritis. However, it will

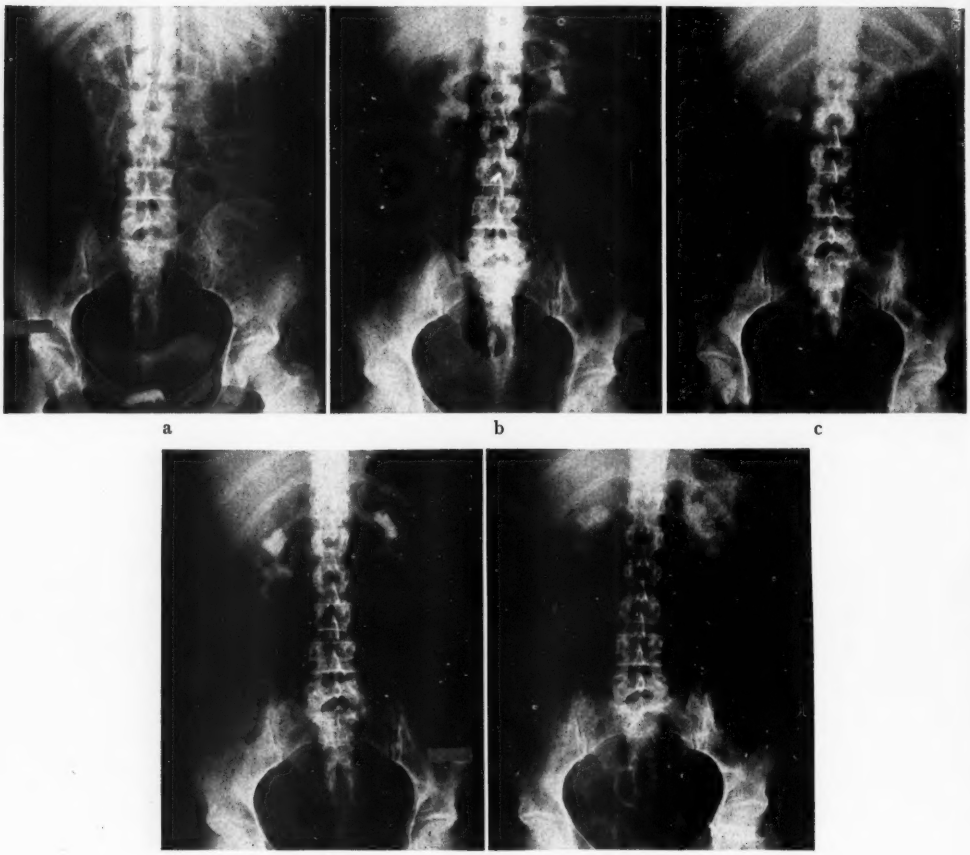

Fig. 2.

be noted that the blood nitrogen levels are elevated in each case, indicating advanced disease with both glomerular and tubular involvement.

On the basis of the data presented it is the author's belief that the following sequence of events occurs in the nondevelopment or development of electrolyte imbalance in ureterosigmoid transplantation:

Patients in normal electrolyte balance. (1) Preoperative kidney function is good. Ureters are transplanted to the sigmoid colon. No demonstrable postoperative infection of the kidneys. (2) Urinary products are absorbed by the colon. However, kidney function is good and is able to maintain homeostasis or electrolyte balance despite colonic absorption of urinary constituents.

Patients who develop persistent electrolyte disturbances immediately following operation. (1) Preoperative renal function is poor. Ureters are transplanted to the large bowel. There may or may not be postoperative pyelonephritis. (2) Urinary products are absorbed by the colon. Because of the poor renal function the kidneys are unable to handle the excessive burden imposed by the absorbed urinary constituents. If the poor renal function is due mainly to tubular damage, then hyperchloremia with acidosis and a normal blood urea

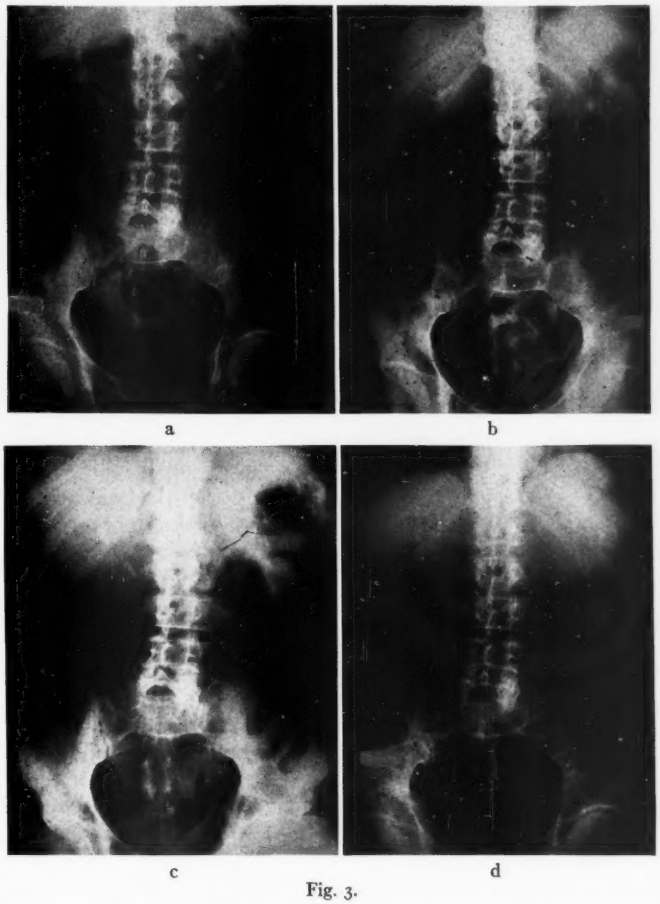

Fig. 3.

nitrogen level will ensue. If glomerular as well as tubular damage is present, then an elevated blood urea nitrogen will develop in addition to the elevated plasma chlorides and lowered plasma bicarbonate.

Patients who develop electrolyte imbalance months or years following operation. (1) Renal function is good preoperatively. Following ureterosigmoid anastomosis patient has occasional intermittent bouts of pyelonephritis. (2) Initially the absorbed urinary constituents are handled with ease by the kidneys and no abnormalities of the cellular environment occur. As more and more tubules become involved by the episodes of pyelonephritis the kidneys gradually deteriorate and lose the ability to cope with the absorbed urinary products; electrolyte imbalance develops. Eventually as the process spreads to the cortex of the kidney, the glomeruli become involved with a resultant decrease in filtration and development of elevated blood nonprotein nitrogen levels. Transient episodes of electrolyte imbalance are probably the result of severe acute episodes of pyelonephritis occurring in an individual with little renal reserve. Subsidence of the acute inflammatory process results in improvement of the renal function with a consequent return to the homeostatic state.

Fig. 4.

In order further to test the validity of the proposed mechanism of electrolyte imbalance in ureterosigmoid transplantation, it was decided to simulate the conditions resulting from ureterointestinal anastomoses in patients with normal and in patients with deteriorated renal function by instilling urine into the rectum. If the proposed mechanism is correct, then one should be able to affect the electrolyte levels in patients with borderline renal function by instillation of urine into the colon; and not be able to create electrolyte imbalance in patients with good renal function. Pertinent experiments are described in Section II.

Section II

METHOD

Six patients were selected for the study on the basis of renal function as determined by urea clearance and phenosulfonphthalein or concentration tests. Three patients demonstrated fairly good renal function and 3 patients poor renal function. Baseline blood chemistry values and nitrogen levels were determined prior to the start of the experiment according to the methods described in Section I.

Each patient was placed on dependent catheter drainage and the urine collected for a period of 3 hours. The total volume of urine obtained over a period of 3 hours from the bladder was then placed in a calibrated flask. Methylene blue was added to the urine for esthetic purposes and also to ascertain whether methylene blue is absorbed by the colon. The flask was then connected to either a No. 32 French Pezzer or whistle tip catheter placed in the rectum. Urine was then allowed to drip into the rectum at a rate calculated to instill the entire volume over a period of 3 hours. At the end of 3 hours the rectal tube was disconnected from the flask and the urine allowed to drain from the rectum. After the rectum had been drained, the rectal tube was then again connected to the calibrated flask which had been refilled with urine that had been drained from the bladder during the previous 3 hours. This process was carried out every 3 hours, night and day, for as long a period as could be tolerated by the patient. It might be mentioned that the tube was removed from the rectum once or twice in every 24 hours for a short period of time for defecation. Blood studies were obtained during the period of urine instillation, and following cessation of urine administration if chemical imbalance had occurred.

In several of the patients an ampule of urokon or diodrast was placed in each 3 hour volume of urine for a period of 24 hours. This was done in order to determine whether it was possible for the urine to reach the cecum under the conditions of the experiment.

RESULTS

The effects of continuous urine enemas on the electrolyte pattern of 3 patients with moderately good renal function are demonstrated in Table VIII.

The values in Table VIII A were obtained on a 70 year old male with a diagnosis of benign prostatic hypertrophy. It will be observed that 7 days of rectal urine instillations did not create any abnormal changes in the electrolyte pattern or the blood urea nitrogen. The methylene blue, placed in the urine which was instilled into the rectum, was readily absorbed by the colon and excreted into the

TABLE VIII.—EFFECTS OF CONTINUOUS URINE ENEMAS ON ELECTROLYTE PATTERN IN PATIENTS WITH GOOD RENAL FUNCTION

A

Procedure and date	Urea clear	90 min. PSP	Concentration test	pH	HCO_3— mEq./L.	Cl— mEq./L.	Protein mEq./L.	Na+ mEq./L.	K+ mEq./L.	Total base mEq./L.	B.U.N. mgm.%	N.P.N. mgm.%
Pre-enema	90%	47%		7.47	28	95	18.3	138	4.9	154	15	
1-19-50—E	nemas started											
1-26-50				7.47	25.7	100	17.1	140	5.2	156	19	
1-27-50—E	nemas discontinued											

rine collected from the bladder; this occurred n all of the patients receiving urine enemas.

Rectal administration of urine over a period f 6 days did not affect the plasma chlorides, he plasma bicarbonate, or the blood nonprotein nitrogen levels in a 64 year old male with urea clearance of 40 per cent and a 90 minute henolsulfonphthalein excretion of 25 per ent; the values are shown in Table VIII B.

The electrolyte patterns indicated in Table VIII C are values obtained on a 62 year old male with good renal function. This patient was very co-operative and tolerated urine enemas for a period of 12 days. It will be observed that electrolyte and blood urea nitrogen values are essentially within normal limits throughout the experiment. The finding of normal electrolyte balance after 12 days of urine enemas is especially significant in view of the fact that some of the urine apparently reached the cecum as demonstrated in Figure 4. It will be recalled that the roentgenogram was taken at the end of a 24 hour period during which time an ampule of diodrast was placed in each 3 hour volume of urine instilled into the rectum.

The results obtained following urine enemas in patients with poor renal function are illustrated in Table IX. The electrolyte values listed in Table IX A were obtained on an 80 year old male with a urea clearance of 22 per cent and 90 minute phenolsulfonphthalein clearance of 9 per cent. Unfortunately, this patient could not tolerate the rectal tube for more than 3 days due to pain from hemorrhoids. However, the urine enemas effected an increase in the nonprotein nitrogen from 45 to 58 milligrams per cent and an elevation of the plasma chlorides from 103 to 111 milliequivalents per liter. The plasma bicarbonate level was not lowered. Two days following cessation of the urine enemas, the nonprotein nitrogen and plasma chlorides had returned to pre-enema levels.

An 88 year old male on permanent suprapubic urinary drainage was selected as an experimental subject; the data concerning him

TABLE VIII

B

Procedure and date	Urea clear	90 min. P.S.P.	HCO_3— mEq./L	Cl— mEq./L	N.P.N. mgm.%
Pre-enema	40%	25%	23.8	102	31
9-25-50—E	nemas started				
9-28-50			25.6	100	36
9-30-50			26.1	104	39
10-1-50—E	nemas discontinued				

TABLE VIII

C

Procedure and date	Concentration test	pH	HCO_3— mEq./L.	Cl— mEq./L.	Protein mEq./L.	Na+ mEq./L.	K+ mEq./L.	Total base mEq./L.	Inorganic P mgm.%	B.U.N. mgm.%
Pre-enema	1.029	7.40	28.3	101	17.9	138	5.3	158	4.3	18
7- 6-50—Ene	mas started									
7-10-50		7.37	27.5	95	17.9	140	5.3	154	4.3	12.1
7-17-50		7.37	28	94	18.3	138	5.5	152	4.2	15
7-18-50—Ene	mas discontinued									

TABLE IX.—RESULTS FOLLOWING URINE ENEMAS IN PATIENTS WITH POOR RENAL FUNCTION

A

Procedure and date	Urea clear	90 min. P.S.P.	HCO_3- mEq./L.	Cl− mEq./L.	N.P.N. mgm.%
Pre enema	22%	9%	25 9	103	45
10-18-50 —	Enemas sta	rted			
10-20-50			27	111	58
10-21-50 —	Enemas dis	continued			
10-23-50			28	104	48

B

Procedure and date	Urea clear	90 min. P.S.P.	HCO_3- mEq. /L.	Cl− mEq. /L.	Na+ mEq. /L.	K+ mEq. /L.	N.P.N. mgm.%
Pre-enema	25%	3%	18.1	105	135	4.8	69
7-19-50—	Enemas	started					
7-27-50			16.8	110	138	4.3	85
7-28-50—	Enemas	disconti	nued				
7-31-50			22.2	106	135	4.9	75
8-4-50			21.8	103			60

are given in Table IX B. It will be observed that the baseline determinations indicate renal function that is beginning to lose its ability for maintaining homeostasis. Urine enemas for 9 days in this patient produced a hyperchloremic acidosis associated with a rise in the nonprotein nitrogen. Seven days after removing the rectal catheter the hyperchloremic acidosis had disappeared and the nonprotein nitrogen level had decreased 25 milligrams per cent.

The electrolyte values in Table IX C were obtained on a 12 year old boy with marked bilateral hydronephroses and hydroureters. The pre-enema electrolyte profile reveals uremia with electrolyte imbalance. After urine had been instilled into the rectum for a period of 5 days, the nonprotein nitrogen had risen from 90 to 173 milligrams per cent; the carbon dioxide combining power had dropped from 15.4 to 13.6 milliequivalents; the chlorides decreased from 117 to 111 milliequivalents; the serum sodium had decreased from 145 to 141 milliequivalents while the serum potassium increased from 5.5 to 6.5 milliequivalents; serum calcium rose and phosphorus decreased. Five days after discontinuing the urine enemas plasma bicarbonate, serum potassium, and inorganic phosphorus had returned to pre-enema levels. The blood nonprotein nitrogen demonstrated a marked decrease from 173 to 132 milligrams per cent after stopping the urine enemas. The serum sodium rose to a higher than pre-enema level while the chlorides remained somewhat lower than the pre-enema level. The enemas were discontinued in this patient because of the onset of nausea and anorexia. These symptoms disappeared within 2 days after cessation of the urine enemas.

DISCUSSION

The experiments described in Section II of this paper were designed to simulate conditions occurring in patients with bilateral ureterosigmoid transplantation, i.e., similar rate of urine entering the colon and evacuation of the urine from the bowel at intervals of 3 hours. Under these conditions instillation of urine into the colons of patients with fairly good renal function did not affect the electrolyte balance nor the blood nitrogen levels. This condition held true even in the patient (Table VIII C) who received urine enemas for a period of 12 days and whose bowel roentgenogram revealed that some of the urine had reached the cecum, supposedly a region with

TABLE IX
C

Procedure and date	Concentration test	90 min. P.S.P.	HCO_3- mEq./L.	Cl− mEq./L.	Na+ mEq./L.	K+ mEq./L.	Ca mgm.%	Inorganic P mgm.%	N.P.N. mgm.%
Pre-enema	1.010	7%	15.4	117	145	5.5	9.9	5.9	97
11-10-50—Enemas	started								
11-15-50			13.6	111	141	6.5	12.3	5.0	173
11-15-50—Enemas	discontinued								
11-17-50			15.4	115	149	5.8	11.3	5.9	127
11-20-50			15.4	112	149	5.5			132

greater powers of absorption than the left half of the colon (6). On the other hand, blood nitrogen levels and electrolyte determinations in patients with poor renal function were definitely changed in 3 to 5 days by the rectal administration of urine. The fact that hyperchloremia with acidosis was not produced in every patient with deteriorated renal function does not invalidate the proposed theory for the mechanism of electrolyte imbalance in bilateral ureterointestinal anastomosis. It is obvious that the organic pattern of renal damage (and thus functional pattern) is probably not the same in each of the subjects utilized since the etiology is different in each of the 3 cases. However, one would expect the same general type of renal deterioration in those patients who have had a bilateral ureterosigmoid transplantation.

Summary and Conclusions

This study was conducted in an effort to determine the mechanism of electrolyte imbalance occurring in many cases of bilateral ureterointestinal anastomoses. The investigation was conducted in two parts. The first section concerned itself with a rather complete postoperative follow-up of 22 patients and 4 dogs who had undergone bilateral ureterosigmoid transplantations. The observations involved excretory pyelography and blood electrolyte determinations at frequent intervals. In addition postmortem studies were conducted on 2 patients and 4 dogs who came to necropsy.

Analysis of the results obtained in the first part of the investigation revealed that 23 per cent of the patients maintained electrolyte balance, normal excretory pyelograms and a clinical condition devoid of episodes of acute pyelonephritis. The remaining 77 per cent gave a history of recurrent attacks of pyelonephritis associated with pyelographic abnormalities and electrolyte imbalance. Hyperchloremic acidosis, the most frequent pattern of electrolyte imbalance encountered, was usually associated with the onset of urographic abnormality and both aberrations were usually preceded by a history of frequent attacks of flank pain and fever. Electrolyte imbalance and urographic abnormality usually appeared months and even years after ureterointestinal anastomoses. The onset of persistent hyperchloremic acidosis immediately after operation occurred in a patient with known preoperative poor renal function. The kidneys of 2 patients and 4 dogs coming to necropsy all revealed chronic bilateral pyelonephritis.

In the second section of this study electrolyte determinations and roentgenograms of the colon were obtained on 3 patients with good renal function and 3 patients with poor renal function who were subjected to continuous urine enemas for a period of days; these patients had not undergone ureterointestinal anastomoses. It was observed that the electrolyte balance of the patients with good renal function was not disturbed by the urine instillations while the patients with poor renal function demonstrated electrolyte imbalance. Roentgenograms of the colon during urine and diodrast administration revealed that urine does reach the cecum.

On the basis of the data presented it was postulated that electrolyte imbalance is due to two factors: (1) poor renal function and (2) intestinal absorption of urinary constituents. Electrolyte imbalance does not occur if renal function is good despite intestinal absorption of urinary constituents; this fact accounts for the patients with ureterointestinal anastomoses who maintain electrolyte balance. Delayed development of electrolyte imbalance can be explained on the basis of gradual deterioration of the kidneys due to recurrent episodes of pyelonephritis. Immediate postoperative development of electrolyte imbalance which persists is due to the fact that the patient's renal function is borderline (in relation to homeostasis) previous to operation.

On the basis of this study the following conclusions have been made:

1. Reabsorption of urinary constituents from the colon occurs constantly following ureterosigmoid anastomosis but hyperchloremic acidosis does not occur if renal function is good.

2. The development of electrolyte imbalance in these cases is determined by the occurrence of impaired renal function.

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URETEROCELE

A Study of 94 Instances in 80 Infants and Children

MEREDITH CAMPBELL, M.D., New York, New York

URETEROCELE, known also as intravesical cyst of the ureter, ureterovesical cyst, or cystic dilatation of the lower end of the ureter, is characteristically a congenital condition mechanically engendered by stenosis of the ureteral meatus with a resulting sacculation of the terminal duct into the bladder (Fig. 1). The wall of the ureterocele sac is composed of vesical mucosa externally and ureteral mucosa internally with a variably scant layer of connective tissue and muscle fibers between. Like most urologists of reasonably wide experience, the writer has encountered a fairly large number of ureteroceles in adults but because of special interest consequent to its congenital nature and great potential gravity in early life, the condition is here considered as we have observed it by personal study and treatment in 80 infants and children with 94 ureteroceles.

ETIOLOGY

A ureterocele must be considered congenital until proved otherwise. The small and often pinpoint ureteral meatus, which induces the ureterocele and behind which it forms, is simply an abnormal localized narrowing of the ureteral channel comparable to similar congenital noninflammatory narrowings which occur not only elsewhere in the ureter, at the bladder outlet, in the urethra, but in the renal calyces as well as in the intestinal, biliary, vascular, pulmonary, and other systems.

Incomplete absorption of Chwalla's membrane has been adduced to explain this narrowing, this explanation being as acceptable as any thus far advanced. Chwalla observed that in embryos 12 to 30 millimeters in length, an epithelial downgrowth or spur membrane formation separates the ureter from the primary excretory duct and produces a physiologic stenosis of the ureteral orifice. Later this membrane bursts or is absorbed and the ureteral orifice becomes patent. Chwalla believes that failure of this process to proceed normally accounts for the various degrees of ureteral meatal narrowing or stenosis so often seen clinically and postmortem; there may even be complete ureteral occlusion here.

Stenosis of the ureteral meatus has been alleged by some to result from local stricture formation consequent to congestive, bacterial, or traumatic inflammation of the bladder wall or perimeatal area as the result of pelvic inflammation, pericystitis, peripheral obstruction, infection, the passage of ureteral calculi or instrumental injury. For example, ureteral meatitis with subsequent scarring and stricture formation has been attributed to adjacent inflammation in the seminal vesicle and broad ligament in the respective sexes (6) with atonic dilatation and intravesical protrusion of the paralyzed intramural ureteral segment. An abnormal intramural course of the ureter has been etiologically cited either as unduly oblique (2) or long and winding (1). Were cystitis alone the factor, the incidence of ureterocele should be much lower in infants and children and far higher in the middle aged and elderly than clinical studies disclose.

On the other hand, all of the ureteroceles here recorded with 1 remotely possible exception were considered by the writer to be congenital, this conclusion being fortified by their high incidence in infants and children, their frequent bilaterality (about 15 per cent as recorded in the literature; 16.3 per cent in the 80 young patients in this series), and their coexistence with other anomalies of the urinary and other systems but notably ureteral reduplication, ectopic ureteral orifice, or congenital stricture elsewhere in the ureters.

Together with the meatal obstruction, a congenital thinning or weakness of Waldeyer's

From the Department of Urology, New York University-Post Graduate Medical School, New York, N. Y.

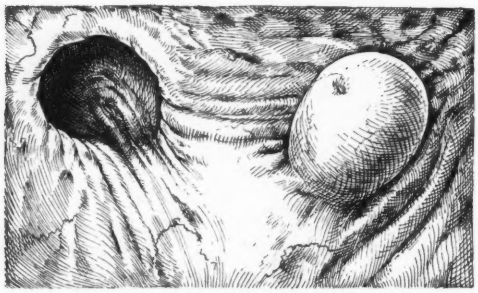


Fig. 1. Ureterocele. Common cystoscopic picture of a small lesion (right); note the minute ureteral orifice on the dome of the cyst. With overdistention of the bladder, the ureterocele frequently everts cystoscopically to simulate a diverticulum (left), and may cause diagnostic error.

sheath (the fibrous envelope of the lower end of the ureter) has been postulated to exist but convincing proof of this is lacking. Nor is such a condition essential to the genesis of ureterocele; rather it well may be the result of ensuing back pressure. As the urine coming down from the ureter meets the impeding meatal stenosis, a back-pressure factor is built up, the total of which is the renal excretory pressure and the hydrostatic pressure of the urine less the relative drainage coefficient of the abnormally small meatal opening. As this force strikes the meatal obstruction, the contiguous ureterovesical mucosa is dilated and ballooned outward, the process proceeding to clinical ureterocele in the manner shown in Figure 2.

INCIDENCE

Ureterocele is found in 1 to 2 per cent of all patients subjected to cystoscopic examination; doubtless the lesion passes unrecognized in some individuals thus examined and there are an infinite number in whom the condition causes no symptoms and examination is not carried out. When complete urologic investigation is performed more often in infants and children with chronic pyuria, a corresponding greater increase in the recognition of ureterocele will be achieved. The unrecognized lesion is sometimes directly fatal in the young through the upper tract damage and the complicating uremia and/or systemic sepsis which it engenders.

TABLE I.—OCCURRENCE

Age	Sex		Side involved		
	M	F	Rt.	Lt.	Bilat.
0— 6 mo.	2	14	8	8	1
7—12 mo.	5	5	3	5	2
13—36 mo.	2	11	6	7	
3— 6 yr.	6	17	6	8	9
7—10 yr.	5	10	6	7*	1
11—15 yr.		2	2		
"Boy"	1			1	
Totals	21	59	31	36	13

*Including 1 case of reduplicated ureterocele on the same side in a 7 year old boy.

Ureterocele was found in 1 of 25 infants and children urologically examined by the writer because of persistent pyuria but was observed in only 4 of 15,919 of this age group examined postmortem. Nor was it recognized (unrecorded) at autopsy in an additional 36,005 bodies over 15 years of age. The last observation is not surprising because the ureterocele collapses after death and is almost certain to be overlooked at autopsy. Moreover, all of these postmortem examinations were either performed or supervised by eminent pathologists in the New York metropolitan area. Indeed, at the operating table, even a large ureterocele may fail to be recognized as it was in an 11 week old boy whose lesion half filled the bladder and prevented urination except in the knee chest position when the cystic mass fell away from the vesical outlet. Although the ureterocele was readily evident in the preoperative excretory urogram but diagnostically passed unrecognized at operation performed by an excellent general surgeon assisted by a urologist colleague, this team could not identify an intravesical cause for the filling defect, overlooked the collapsed ureterocele, and even mobilized the bladder completely, vainly to investigate the subvesical area for tumor, cyst, or other extravesical condition which then was thought must exist to account for the cystographic filling defect. Suprapubic drainage was established. Yet 2 weeks later when the infant was seen in consultation, the enormous ureterocele was cystoscopically demonstrated; incision to establish free urinary drainage and catheterization were carried out. This experience is cited to stress both the importance of cystoscopic diagnosis in ureterocele and the

extreme difficulty of casually identifying the collapsed lesion at the operating table or post-mortem and especially when it is small or only moderately large. Morever, a collapsed ureterocele may be cystoscopically overlooked!

The age, sex, and side of involvement factors in the cases here reported are indicated in Table I. In a 7 year old boy there were 2 large ureteroceles on the left and corresponding to the orifices of the reduplicated left ureters, each of which drained a massive infected megaloureter and pyonephrotic pelvis of the destroyed kidney above. On the right side in this case, a congenital stricture of the lower third of the right ureter and congenital contracture of the vesical outlet coexisted.

PATHOLOGY

Ureterocele may be classified as follows: (1) Simple (usual): (a) unilateral; (b) bilateral; (c) reduplicated on same side (i) without fusion, (ii) with fusion; (d) with compression of adjacent reduplicated ureter; (e) with compression of contralateral ureter. (2) Prolapsed: (a) in female (to urethra or externally); (b) in male (to prostatic urethra). (3) Ectopic opening: (a) in urethra; (b) in vesical diverticulum. (4) Blind-ending intravesical cyst.

The clinical importance of ureterocele is primarily the renal injury caused by urinary back pressure and, nearly always, complicating infection. As the obstruction persists, not only does the ureterocele enlarge, but there is progressive dilatation of the ureter and renal pelvis above, often with the production of megaloureter, massive hydronephrosis, and even total renal destruction (Fig. 3). Occasionally the upper tract is urographically normal or the changes are relatively minimum, even with a fair sized ureterocele, but here the meatal obstruction is comparably mild.

Hydronephrosis as urographically demonstrated in the 80 infants and children is shown in Table II. In this computation are included not only the bilateral hydronephroses in bilateral ureterocele, but also those hydronephroses of various causation contralateral to ureterocele. The degree of ureteral dilatation (ureterectasis) in these cases is also shown in Table II. The explanatory statistical note just given for hydronephrosis comparably

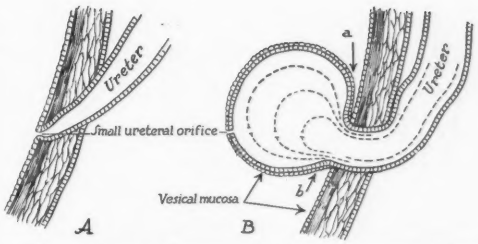


Fig. 2. Genesis of ureterocele: A, small ureteral orifice; B, progressive stages in the ballooning out of the vesical mucosa. When the orifice is at the sites (*a*) or (*b*) there is asymmetrical ballooning with the meatus respectively on the upper or underside of the ureterocele; in my experience these hidden orifices are more often on the upper posterior surface.

applies here. Dilatation of the upper urinary tract in ureterocele associated with ureteral duplication is considered under reduplicated kidney. The striking and vitally important observation is the high incidence of far advanced hydronephrosis and ureterectasis in this series which is sufficiently large accurately to reflect the gravity of ureterocele and its complications, especially in the young.

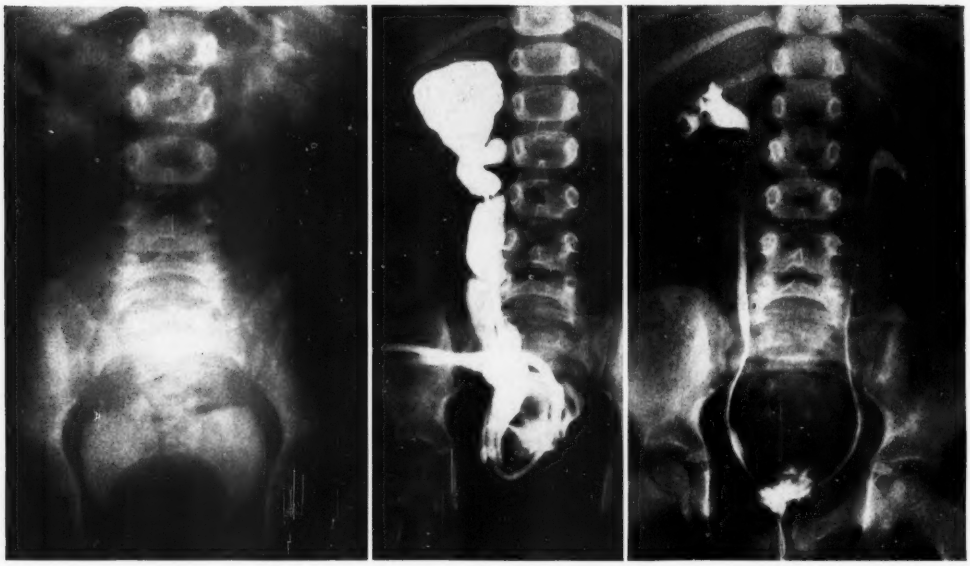
Infection may be anticipated in every case; chronic grossly evident pyuria was the principal manifestation for urologic examination in 51 of the 80 children in this series.

Stone formation is favored by both the urinary stasis and infection and was found in 6 cases examined. In a 25 year old woman, a 40 year old man, a 5 year old boy, and a 3 year old girl ureteral calculi localized in the cystic dilatation, their expulsion being prevented by

TABLE II.—PATHOLOGY

Hydronephrosis*	
None	26
+	14
++	7
+++	8
++++	34
Not stated	5
Grossly infected	32
Hydroureter*	
None	25
+	10
++	8
+++	8
++++	41
Not stated	2
Size of ureterocele	
Unilateral	
Large	28
Small	30
Not stated	4
Bilateral	
Large	10
Small	18
Not stated	4
Caliber of orifices	
Tight	16
"Minute"	13
Patent	14
Small	9
Gaping	1
Not found	1
Prolapsed	6
Protrusion into urethra	3

*Of segment drained by the ureterocele.



A B C

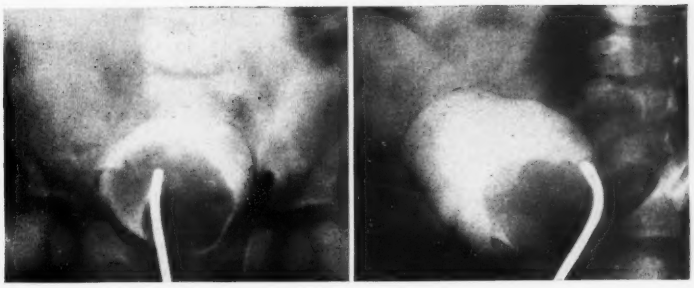
Fig. 3. Ureterocele in a 22 month old girl examined because of chronic pyuria. A, Excretory urography showing normal left upper urinary tract with a mildly dilated lower segment of a reduplicated right kidney. Negative shadow in the cystogram outlines the ureterocele of the ureter which drained the greatly dilated right upper ureterorenal segment (B). Treatment: right ureteroheminephrectomy; transvesical ureterocelectomy. C, Right lower reduplicated renal segment remaining following ureteroheminephrectomy. Cured.

the stenosed meatus of the ureterocele. A large branching coral stone filled the pelvis of a dilated pyonephrotic left kidney in a 2 year old girl in whom ureteronephrectomy above a ureterocele with a tight meatus was demanded. Similarly in a 2 year old boy with a right ureterocele (tight meatus) and greatly dilated ureter and pelvis above, ureteronephrectomy was performed because of persistent hyperacute renal infection, so-called persistent acute pyelitis. To our surprise, the renal pelvis was found filled with stones, none of which was suggested by either the plain scout roentgenogram or the retrograde pyelogram.

Most ureteroceles are round or globular in outline but they may be oval, elongated, or broad and flat. In the pyriform variety the meatal opening is often ectopic in the urethra.

Ureteroceles vary greatly in size, not only as observed during the filling and emptying cycle as described under diagnosis, but also as to their maximal capacity as indicative of the magnitude of the lesion. Thus the ureterocele may be not over 1 centimeter in diameter or it may completely fill the bladder, notably in the young, and as it did in 6 of our cases (Fig. 4). In 6 females in this series, the ureterocele prolapsed through the urethra to simulate eversion of the bladder from which the condition must be differentiated. In 3 other cases the ureterocele protruded into the deep urethra. In 14 cases the lesion effectively obstructed the vesical outlet.

Rarely, as in 3 cases treated by the writer by suprapubic excision, the intraureterocele hydraulic tension was so great as firmly and completely to compress the intramural segment of the accompanying reduplicated ureter or even the adjacent contralateral ureter which consequently showed advanced hydroureter and hydronephrosis. With incision of the tense ureterocele and release of the pressure that its content exerts on the adjacent ureter, the latter at once completely empties



A B

Fig. 4. Ureterocele of ureter draining upper segment of reduplicated right kidney in a 1 year old girl examined because of chronic pyuria. A, Anterior posterior cystogram. B, Lateral cystogram. Ureteroheminephrectomy and suprapubic ureterocelectomy. Cured.

itself with an enormous gush of dammed-back urine. In 1 of these cases, a 12 month old boy, this urine was mahogany color from old blood; the infant had been referred for urologic investigation and treatment because of hematuria subsequently proved to originate in the intensely congested contralateral upper tract secondarily obstructed by compression of the ureterocele of the reduplicated ureteral mate.

When the ureterocele is small or only moderately large the minute meatus will generally be found on the anterior or anterosuperior aspect of the cyst, i.e., directly as the cystoscopist looks at it (Fig. 1). With greater increase in size of the lesion or because of early distortion in the genesis of the ureterocele, the meatus may be found on the under, lateral, median, or posterior surface. In some cases of meatal displacement, the orifice cannot be found because of technical cystoscopic difficulties and even with chromocystoscopy. Rarely there is no meatus (congenital intravesical cystic dilatation of a blind-ending ureter).

Anomalies of the urogenital and other systems commonly coexist with ureterocele. Isolateral complete ureteral reduplication was found in a third (27 or 33.7 per cent) of our 80 cases in children (Fig. 3). Unilateral complete ureteral reduplication occurred in 16 cases (right, 11; left, 5; and bilaterally in 11). Contralateral ureteral reduplication was complete in 10 and incomplete in 1. In an additional case the reduplication was incomplete on the side of the ureterocele, but complete on the opposite side. In 3 girls, 3 months, 13 months, and 2 years of age, the ureterocele extended down the floor of the urethra as a tube to open in the posterior third. In each child the upper tract drained by the ureterocele was dilated and in 1 of these bilateral ureterocele was found. In a child of 13 months who was admitted to the hospital *in extremis*, excretory urography suggested bilateral ureterovesical junction stricture with massive bilateral hydroureter and hydronephrosis above. Bilateral nephrostomy was performed at once to establish free urinary drainage; a second ureter on the right side which opened into a large ureterocele was not recognized at the operating table but was discovered postmortem. In 4 cases the orifice of the accompanying reduplicated ureter was ectopic, in the urethra in 3 (Fig. 6), and in the introitus in 1. In 1 girl the urethral opening was ectopic on the vaginal roof—a severe degree of hypospadias. In a 13 year old girl examined because of hematuria, the blood was observed to come from the hypoplastic kidney above a small tight right ureterocele.

Urologic examination of the upper urinary tract of the young patients reported in this series showed it to be normal in 40 (right, 15; left, 12; bilateral, 13); in 7 the ureter was dilated but the pelves were normal. Ureteral stricture on the side of the ureterocele was found in 27 cases (right, 10; left, 12; bilateral, 15); the reduplicated ureter isolateral with the

Fig. 5. Large ureterocele partially filling the bladder in a 6 year old girl examined because of persistent pyuria. The ureterocele which is demonstrated here positively by urographic filling and appears as a bladder-like structure of the "cobra head" or "spring onion" morphology drained the enormously dilated and infected left upper reduplicated renal segment. The dilated ureter of the isolateral lower segment was obstructed by pressure of the ureterocele mass, and the right upper urinary tract was dilated above a congenital ureterovesical junction stricture.

ureterocele showed stricture in 15 cases. Secondary kinking was observed in 9 cases; ureteral tortuosity in 24 cases, with pronounced angulation in 7.

The opposite kidney was congenitally malascended, hypoplastic, or showed aberrant vessel obstruction in 2 cases each. The contralateral kidney showed ectopia, supernumerary renal buds, vascular anomalies, agenesis, multilocular cystic disease and aplasia in 1 case each. In 4 cases the opposite kidney showed hydronephrotic atrophy and in 1 case each sclerosis (renal rickets), renal embryoma, ureteropelvic fibrosis, stone, cortical abscesses, sclerotic nephritis, and massive suppuration.

Examination of the bladder showed it to be normal except for the ureterocele in 24 cases. Varying degrees of cystitis existed in 27 with marked vesical edema in 9. Other findings with their incidence are shown in Table III as are the lesions encountered in the urethra.

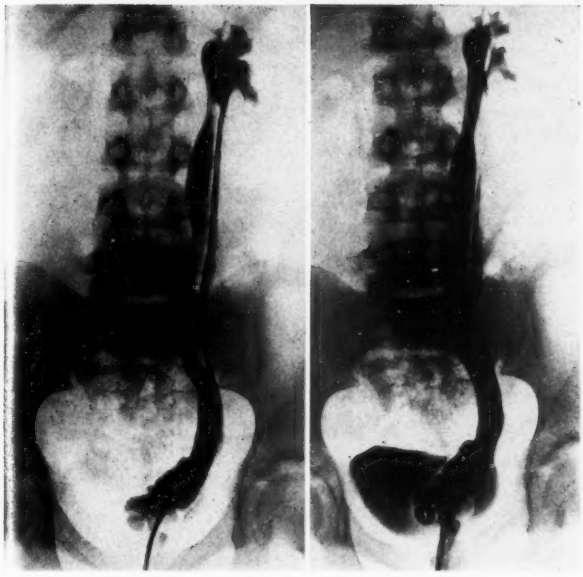
Demonstrated anomalies of other body systems in these children included pronounced spina bifida (4), fused labia minora (3), and 1 case each of clubfoot, absent anus, diaphragmatic hernia, umbilical hernia, retarded mental growth, pyloric stenosis, convergent strabismus, patent foramen ovale, accessory spleen, ependymal rest, and 1 child had congenital syphilis.

In view of this incontrovertible association of ureterocele with other coexisting developmental defects in the same individual, it is reasonable always to consider the intravesical cyst as congenital and at least until definitely proved otherwise. The writer has encountered but 1 ureterocele that suggested other than a congenital origin. This occurrence in a 4 year old girl with an enormous ureterocele was etiologically questioned because the orifice gaped slightly.

SYMPTOMS

The clinical manifestations of ureterocele reflect both the urinary obstruction and vesical irritation, caused by the lesion, and infection. Two-thirds of these patients (51) were referred for urologic examination because of persistent macroscopic pyuria, with or without continuous or recurrent fever (45). Additional urologic symptoms present either singly or in various combinations in our patients were: frequency of urination (18), hematuria (17), dysuria (15), urgency (9), and vesical distress. Frequency of urination, dysuria, urgency, or even incontinence may be caused by irritation of the ureterocele mass itself in the bladder and especially when it is near the vesical outlet; or it may be due to congestive inflammation, infection, or both. Sometimes there is simply a feeling of fullness in the bladder after voiding. In 6 cases, vesical retention was recurrent and in 3 cases acute because the cyst obstructed the bladder outlet in ball-valve fashion. In some cases of chronic complete vesical retention, paradoxical or overflow incontinence occurs; in 3 cases it had been clinically designated as enuresis.

Pain is present in many cases but is seldom the only symptom. It is usually isolateral with the ureterocele and exists as a pain or ache in the side or renal region; it reflects



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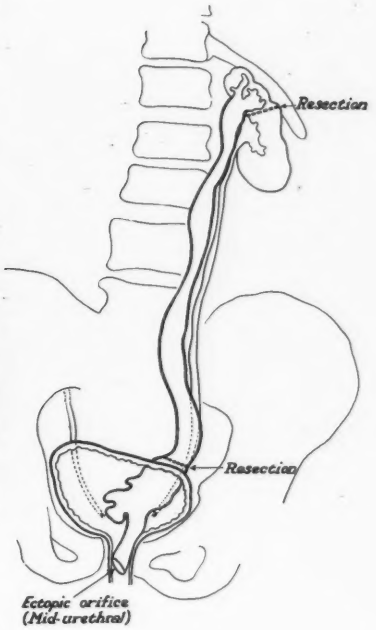

C

Fig. 6. Lobulated ureterocele of the reduplicated upper segment of the left upper tract opening ectopic in the anterior urethra of a 22 month old girl with persistent pyuria. A, Reduplicated left upper tract showing dilated upper segment and normal lower segment. B, Ureterocele cystographically outlined. C, Conditions present; ureteroheminephrectomy. Cured.

either urinary back pressure or infection but commonly both are present. Yet in 14 cases, the pain was abdominal and predominantly in the lower segment; in 3 of these cases the mass of chronic vesical overdistention was readily palpable.

Because of the frequent coexistence of other urinary tract anomalies and diseases with ureterocele, and notably of the opposite side, as has been previously discussed with statistical citation, the symptoms may be referable to either isolateral or contralateral lesions such as ureteral stricture, infected hydronephrosis and so forth.

When prolapse of the ureterocele through the female urethra occurs as it did in 6 children of this series, acute urinary retention nearly always ensues, but is immediately relieved by replacement of the cyst to the bladder. In the male, prolapse extends only into the prostatic urethra. In a 5 week old girl in whom the chronic urinary retention was not recognized to result from complete obstruction by a prolapsed ureterocele, another surgeon, in the absence of adequate examination, had performed suprapubic cystostomy. When she was seen at 7 months of age and with the suprapubic drainage still functioning, cystoscopic examination disclosed the vesical outlet to be

TABLE III.—OTHER FINDINGS

Bladder		Urethra	
Normal except for ureterocele	24	Urethrotrigonitis	14
Cystitis (varying degrees)	27	Stenosis external meatus	8
Marked edema	9	Stricture elsewhere	8
Severe trigonitis	3	Abnormally small urethra	4
Trabeculation	14	Valves	1
Saccules	2	Hypospadias in female	1
Contracted neck	8	Marked phimosis	2
Diverticulum	8		
Marked dilatation	8		
Hypertrophy of trigone	4		
Narrow outlet	3		
Palpable distention	3		
Residuum	11		

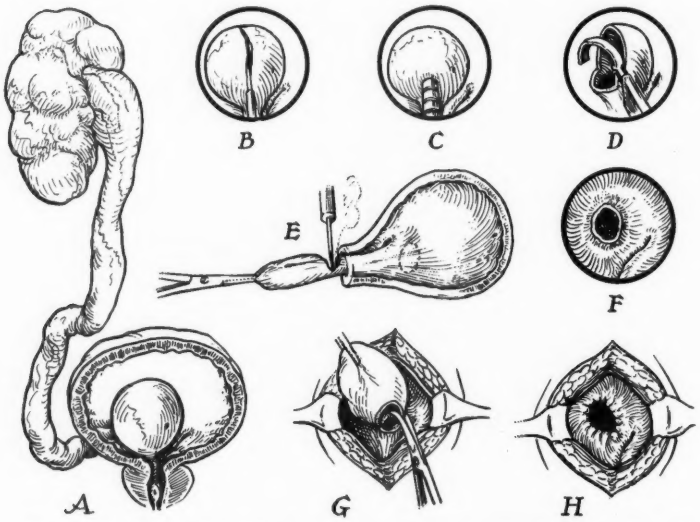

Fig. 7. Treatment of ureterocele. A, Appearance of a small ureterocele which drains a greatly dilated ureter and renal pelvis. B, Cystoscopic division of the ureterocele by an electrode. C, Cystoscopic dilation of the ureteral orifice by the passage of a large bougie, a method which is almost always fruitless. D, Transurethral resection with wide removal of the crown of the ureterocele or, preferred, of the entire structure, leaving a wide open ureteral orifice in the bladder (F). E, Treatment in the female by passing slender forceps through the urethra into the bladder to grasp the ureterocele and pull it out as far as possible; division with scissors, knife, or, best, cautery is shown. G, Suprapubic excision of ureterocele. H, A running hemostatic suture is taken about the base, but topical hemostasis with ligation is better. The simplest procedure is D, yet in the very young the size of many of these lesions and technical instrumental considerations and handicaps commonly make suprapubic excision the safer operation.

completely occluded in ball-valve fashion by an enormous left ureterocele which was removed. Yet, in the interval, the kidney had been permitted to suffer continued and progressive damage by the obstructing ureterocele. Moreover, when the vesical outlet is obstructed by the cyst with or without prolapse and in both sexes, the entire upper urinary tract is bilaterally injured by back pressure and, as a rule, by complicating infection.

The systemic manifestations of the complicating urinary infection generally cause the diagnosis of "acute" or "chronic pyelitis" to be made (see diagnosis). Chronic urinary infection in these cases must always be considered to be predominantly renal, the toxemia of which is reflected in gastrointestinal disturbances, often pronounced, with vomiting (18), anorexia (15), malaise, headache (7), "indigestion," constipation (7), diarrhea (5), loss of weight (7), failure to gain (7), and/or progressive anemia. In 42 the complaint was chronic illness, in 28 it was "chronic urinary trouble," 10 were acutely ill, and 5 had convulsions. With advanced bilateral renal injury by back pressure and infection, unrelieved, the patient may die in uremia or urinary sepsis, as occurred in 6 cases in this series first seen *in extremis* or at least desperately ill.

DIAGNOSIS

A careful physical examination of the patient prior to instrumental urologic investigation is essential and may reveal a distended bladder, renal tenderness, abdominal tenderness or rigidity, a urethral mass, a prolapsed ureterocele, excoriation of the genitalia, labial fusion, or other findings suggestive of urinary tract disease. Anemia and malnutrition are commonly manifest, especially when the uri-

nary infection has been of long duration; there may be general underdevelopment or even dwarfism.

The next investigative step should be urinalysis and bacteriologic study (culture or Gram's stain of centrifuged sediment). Collection of the urine specimen should be by catheterization in females of all ages, and by this method in males as well if a satisfactory collection from the voided stream cannot be made. Urinalysis findings in specimens thus initially collected from the patients in this series and, following treatment, the last time the patient was seen are shown in Table IV. Similarly the bacteriologic study of the urine by culture before and after treatment is recorded in Table IV.

TABLE IV.—URINALYSIS FINDINGS

	Initial examination	Last examination (after treatment)
Urinalysis		
Normal	9	35
Turbid	29	
Albumin (++++, 10)	37	12 (++++, 4)
Sugar	1	0
White blood cells (pus) (++++, 24)	46	17 (++++, 5)
Red blood cells (++++, 5)	31	5
Casts	18	2
Incomplete	5	5
Urine culture		
Sterile	7	29
Bacillus coli	45	7
Bacillus proteus	4	2
Ps. pyocyanea	4	4
Staph. aureus	42	13
Streptococcus	27	11
Bacillus subtilis	1	0
Mixed	38	4
No report		7

A complete urologic examination is indicated in patients of all ages who present the symptoms noted in the adjacent preceding paragraphs. A preliminary cystographic or, better, an excretory urographic study will often disclose a vesical filling defect caused by the ureterocele (Figs. 3, 4). This was achieved in 35 of the 41 cases in which the method was used; in the remaining 6 cases the vesical outline appeared normal in the excretory cystogram. It is notable that in all but 8 of these cases the cystogram—abnormal with filling defect preoperatively—postoperatively was normal. When the excretory method is employed, early films will commonly show splendidly outlined the dilated ureter and renal pelvis above the ureterocele with a bulbous "cobra head" or "spring onion" filling outline of the intravesical cyst itself (Fig. 5). When the ureterocele is enormous and fills the bladder, the cystographic shadow may appear only as a halo around the ballooned ureterocele, the radiographic medium finding only the space between the cyst and the bladder wall. With the ureterocele filled with contrast medium but the bladder uninjected, the cyst may be seen to fill the viscus which will be outlined as a darkened shadow. Rarely the ureter will be urographically seen to be sharply cut off at the bladder wall and without filling of the intravesical cyst.

Cystoscopic examination. A competent cystoscopist is unlikely to overlook a ureterocele. Yet it may easily be missed if the observation is made when the cyst is collapsed. Ureterocele usually presents a classic picture; as the cyst rhythmically fills with urine under peristaltic projection, it expands into a ballooned, semitranslucent, easily indentible mass which collapses as the urine slowly empties through the small meatus into the bladder. The covering of the cyst is bladder mucosa in which, when uninflamed, the usual network of blood vessels is readily seen. Often the stream of urine can be seen being ejaculated from the minute meatus. When the meatus is unusually small and tight and, as a corollary, the cyst is apt to be large or enormous, the ureterocele may not be able to empty itself between the ureteral peristaltic deliveries of urine. It remains constantly distended as a large soft mass reflecting the peristaltic ureteral contractions, a feature which may make discovery of the ureteral orifice difficult or impossible, especially when it is beneath or far on the posterior aspect of the cyst, and even though indigo carmine has been given intravenously for meatal chromocystoscopy. In many of these cases and failing to find the orifice, the diagnosis of congenital blind-ending ureteral

cyst is made, which may be accurate but more often is not. Seldom, if ever, should the cystic lesion be confused with neoplasm such as carcinoma or fibroma.

When the meatus of the ureterocele cannot be found or catheterized, or the excretory urogram is of no aid because of inadequate renal function on the involved side, the ureterocele and urinary tract above can be urographically demonstrated by the injection of skiodan or other radiopaque medium employed for excretory urographic study. The injection is made through a hypodermic needle fastened to the tip of a ureteral catheter and cystoscopically introduced through the wall of the cyst as suggested by Mertz, Hendricks, and Garrett. I have found it simpler to incise the cyst wall with miniature cystoscopic scissors, introduce the ureteral catheter through the new opening, and perform retrograde pyelography in the usual manner.

The diagnosis was made by preoperative cystoscopy in 74 of the 80 cases here reported; in the others the cystographic vesical filling defect denoted the ureterocele. Preoperative retrograde pyelography was performed in 60 of the 74 children cystoscopically examined; in the remaining 14 cases, the ureterocele meatus could not be found or, catheterized, the catheter coiled in the ureterocele sac and did not go up the ureter. Yet in some cases in which the ureterocele could not at first be catheterized, retrograde pyelography was achieved after incising the ureterocele. It is of interest that in the urologic examination of these infants and children, anesthesia was unnecessary in a third (26); inhalation anesthesia —chiefly vinethene—was used in 30, intravenous anesthesia in 14, and in 21 the type of anesthesia employed (office) was not stated. Yet it is probable that in at least half of the last group, no anesthesia other than codeine sulfate was employed.

In 5 cases the dilated upper urinary tract above the ureterocele was demonstrated by pyelographic injection through nephrostomy tubes, employed because of far-advanced obstructive renal injury.

In nearly every case of ureterocele sufficiently advanced to cause symptoms, dilatation of the ureter and renal pelvis will be demonstrated; often the ureterectasis and hydronephrosis are extreme even with destruction of the kidney parenchyma and complete loss of renal function (Figs. 3, 6).

With cystoscopic overdistention of the bladder, it is not unusual for the ureterocele to evaginate in diverticulum formation as noted in 11 of our cases (Fig. 1). Sometimes the meatus not previously found will then be identified on the interior of the sac cavity. In a 5 year old girl examined because of persistent pyuria and in whom this situation was encountered, the stenosed meatus was readily and widely incised with miniature cystoscopic scissors to establish free urinary drainage.

Cystitis is commonly observed in these patients, as indicated in Table III, and may vary from mild to severe.

Prolapse or simple eversion of the ureteral mucosa is usually induced by the passage of a stone and appears as a simple mucosal extrusion through the orifice. Rarely do the outer layers of the ureteral wall participate in the process. Finally, the prolapsed tissue is covered by ureteral mucosa while a ureterocele is covered by vesical mucosa.

The ureterocele recently prolapsed through the female urethra is recognized as a greatly congested fiery red mucosal mass ballooning from the meatus; if the prolapse has existed many hours, the surface of the prolapsed cyst may be dull red and, still later, there may be suggestion of severe interference with the blood supply. Ureterocele prolapse is to be distinguished from urethral prolapse; the last appears as an eversion rather than as a ballooning and lacks the fine vascularity of the bladder mucosa which covers the ureterocele. In prolapse of the bladder, the thickness of the vesical walls in contrast to the thinness of ureterocele walls is distinguishing; often the entire trigone and ureteral orifices may be identified in simple vesical prolapse. This condition occurred in an infant girl 2 weeks following transurethral removal of a large right ureterocele, and was immediately and uneventfully reduced.

TREATMENT

The therapeutic objectives are eradication of: (1) obstruction and (2) complicating in-

fection, stone, and other conditions. The various methods for the treatment of ureterocele are shown in Figure 7.

1. Cystoscopic dilation of the stenosed ureterocele is rarely adequate treatment because of prompt recontraction, and in infants and children there are added instrumental limitations consequent to the small caliber of the urethra and especially in young males (Fig. 7). The method is not recommended. In the series of children here reported, ureteral dilation was employed only in conjunction with ureteral meatotomy and never as the only method of treatment. Postoperatively ureteral dilation was employed unilaterally in 11 cases and bilaterally in 18.

2. Cystoscopic division of the ureterocele or wide meatotomy is usually effective in removing the obstructive factor. The writer's 17 F. ureteral dilating and operating cystourethroscope employing miniature meatal scissors or ureterotome will be found most useful for this procedure. The ureterocele can be similarly divided by the cutting electrode as it was in 2 of our young patients (Fig. 7, B). Often the ureterocele can be completely bisected following which its two halves will retract, leaving a widely patent ureteral orifice. This procedure was employed in 16 of the cases here reported. Unless the newly established drainage is complete, not only will urinary stasis remain in the tract above but there is poor chance of sterilization of the urine, even with modern chemotherapy and antibiotic therapy.

3. Ureterocelectomy through the open bladder is a most satisfactory procedure and was performed in 25 of our cases in infants and children (Fig. 7, G). This operation merits employment chiefly when there are other lesions, such as ureterovesical junction stricture of another ureter which is best treated by open surgery, and both conditions are attended to at the same sitting. A ureterocele large enough to protrude through the urethra is usually best excised suprapubically and especially in the young, or if the prolapsed segment has been strangulated. Only rarely does the base of the excised ureterocele require running suture hemostasis (Fig. 7, H). In placing the suture, care must be observed not to include an adjacent lower ureter. Topical ligation of individual bleeding vessels is preferred.

4. In 2 cases, girls of 2 and 4 years, a small Kelly clamp was introduced through the urethra into the bladder to grasp the ureterocele and pull it out through the urethra where it was cut off with scissors (Fig. 7, E). A knife could also be used, but probably electrocautery cutting for its coagulating effect would be best. The thin-walled ureterocele is readily distinguished from the thicker-walled bladder proper. A small balloon catheter is left indwelling in the bladder for at least 2 days. In a third case, a girl of 5 years in whom this procedure was attempted, the ureterocele could not be satisfactorily delivered through the urethra; it was treated by transurethral resection.

In our limited experience with this method which I have not found previously described, there was blood-tinged urine for a day; a most satisfactory result was achieved in each case. Undue bleeding demands prompt hemostasis by cystoscopic electrocoagulation.

5. Transurethral excision of the ureterocele, using either the adult or miniature resectoscope according to the size of the patient and the urethral caliber, is the best treatment in most cases (Fig. 7, D). Either the Stern-McCarthy resectoscope or the Nesbit modification of it is used; I prefer the Nesbit instrument, When the caliber of the urethra of the young male with ureterocele does not permit passage of the 16 F. miniature resectoscope for transurethral resection of the intravesical cyst, the instrument may be readily introduced through a perineal urethrostomy opening.

In transurethral excision as employed in 11 of the children here reported, the ureterocele is progressively whittled away, beginning with a long bisecting incision of the cyst; the margins of the divided lateral halves are next excised strip fashion nearly to the bladder wall (Fig. 7, D). Electrocoagulation achieves hemostasis. A small balloon catheter may advisedly be left in the bladder for 48 hours following the operation. In a 35 year old male with recurrent urinary difficulty and frequency due to a large (3.5 cm. diameter) left ureterocele, excision of the lesion with the

Stern-McCarthy resectoscope was followed 3 days later by profuse postoperative hemorrhage. This responded promptly to indwelling catheterization. In Cowen's case retrocystic perforation of the juxtavesical ureter followed division of the ureterocele with a Collings' electrode, the complication being attributed to dispersal of the electrocutting current over the surface of a stone in ureterocele cavity.

When the stone is present in the ureterocele cavity, division of the cyst must be ample to permit passage or instrumental extraction of the calculus and was successful in 2 of our patients. Yet in a 5 year old boy with a calculus 8 millimeters in diameter lodged in the lower ureter, following inadequate incision of the ureterocele, the stone passed downward to impact in the newly made orifice which seemed ample at the time but became contracted by edematous swelling. Acute focal suppurative nephritis with fulminating sepsis promptly followed the sudden complete ureteral obstruction and demanded emergency ureteronephrectomy. This was followed by retroperitoneal abscess secondary to leakage of infected urine (vesicoureteral reflux blowout?) from the ureteral stump. The abscess was drained, but the boy died 1 week later following intestinal evisceration through the infected loin wound.

When the ureter is adequately opened to permit free urinary drainage and despite virtues attributed by some to limited division of the cyst, vesicoureteral reflux usually ensues but is seldom of great clinical concern. Unquestionably it injures the kidney less than did the previous obstruction.

Ureteronephrectomy is demanded when the tract, and notably the kidney above the ureterocele, is hopelessly injured; it was employed in 21 of our patients treated by open surgery and with subsequent removal or wide incision of the ureterocele. The ureter is removed down to the bladder wall or as near to it as technically possible. Less than total ureterectomy is certain to leave a variable pyoureter—in essence, an infected diverticulum—which will continuously pour infected urine into the bladder and jeopardize the "good" ureter and kidney. In 4 instances it was necessary to perform secondary removal of the remaining pyoureteral stump.

Coexisting anomalies commonly demand surgical correction in conjunction with treatment of the ureterocele. When the ureter draining through the ureterocele is a reduplicated structure, ureterocelectomy and, generally, ureteroheminephrectomy are required as in 13 of these cases. Most often the pathologic segment is the upper half of the ureterorenal reduplication as it was in 17 of our cases; the lower half was involved in 3, both segments were diseased in 4, and in 3 the site was not recorded. The condition of the patient at operation may demand a two stage procedure with initial incision and drainage of the ureterocele and later, when the patient is more fit, ureteronephrectomy or ureteroheminephrectomy is carried out. Nephrectomy alone was employed but once.

Additional surgical attacks on the upper urinary tract include nephrostomy (temporary in 2, permanent in 3); ureteral resection, 4; ureterolysis, resection of aberrant vessels, and ureteroneocystotomy, each 2; ureteropelvioplasty and renal exploration, each 1. Indwelling catheterization was temporarily employed in the ureter in 8 cases and in the bladder in 12.

Anomalies and other lesions of the bladder or its outlet required treatment as follows: cystotomy (temporary 9, permanent 4); bladder neck resection (transurethral, 7; suprapubic and punch operation, each 2); bladder resection, diverticulectomy, and reduction of prolapsed bladder, each 1; urethral meatotomy, 6; urethral dilation, 31; perineal urethrostomy for cystoscopy or transurethral resection, 3; transurethral resection of hypertrophic verumontanum and urethral valves, each 1, and punch operation for prostatic urethral valves, 1.

No patient with urologic disease can be considered cured as long as urinary infection exists. Various forms of sulfonamides were administered in 60 cases, mandelic acid compounds in 13, antibiotics in 58, methenamine in 8, and combined therapy in 36. That urinary sterilization may be achieved in many of these cases is indicated in the previously given tabulation (Table IV) of the urinary findings.

That the general condition of the patient as well as the treatment of his disease merits

close attention is reflected in the fact that nearly all of these children undergoing surgical therapy received blood transfusions.

Periodic postoperative examination of the patient is essential to be certain (1) that the therapeutic results have been adequate, (2) that an incised ureterocele still drains freely, (3) that there are no other or previously unrecognized urologic lesions which demand attention, and (4) that the urine remains sterile.

PROGNOSIS AND RESULTS OF TREATMENT

The prognosis is dependent upon the degree of renal damage, infection, stone, and other conditions associated with or secondary to the ureterocele. The more advanced the urologic injury when the diagnosis is made and treatment is undertaken, the poorer the prognosis.

With the establishment of free urinary drainage or complete eradication of all obstruction, improvement in renal function often follows, and particularly when coexisting urinary infection is controlled or eradicated, the prognosis is correspondingly improved. When the restitution of renal function seems unlikely or is not achieved and infection cannot be eliminated, ureteronephrectomy or, when indicated, ureteroheminephrectomy is demanded which, when the disease is unilateral, is almost always followed by prompt improvement. In bilateral involvement the prognosis is generally grave. Yet in all cases the employment of modern chemotherapy and antibiotic therapy will not only lessen the over-all morbidity but will save some lives. In retrospect, it seems certain that some of the children in this series who died could have been saved had present-day antibiotic therapy been available.

Of the 35 cases treated by cystoscopic procedures, 9 were cured, the obstruction having been relieved and the urine sterilized. Twelve others in this group were improved, 6 were unimproved, and the end result in 5 is uncertain. Three died of nonurologic disease, pneumonia in 2 and following subsequent operation for diaphragmatic hernia in the third. Of the 45 treated by open surgery, 13 were cured, 18 were improved, 4 were unimproved, the end result is unknown in 2, and 8 died. In short, 52 or nearly two-thirds of these infants and children, many of whom were desperately ill and with complicated surgical problems, were either cured or improved. Complications, infection, obstruction, stone, and sepsis were directly fatal in 6 children, all of whom were operated upon. Four of the 6 children dying postoperatively were *in extremis* with urosepsis when admitted to the hospital. Another child died with urinary sepsis complicated by barbiturate poisoning, a sixth child died following intestinal evisceration through an infected loin wound, and 2 died of pneumonia.

SUMMARY

Ureterocele is an obstructive congenital anomaly.

It is not uncommon, being found in 1 to 2 per cent of all individuals subjected to cystoscopic examination and in our series of children with persistent pyuria was identified in 3.5 per cent.

Secondary infection is the usual and most important complication; unfortunately it is generally dismissed temporarily with the diagnosis of chronic pyelitis. Meanwhile urinary antisepsis is generally fruitless and back-pressure damage of the ureter and kidney above the ureterocele progresses. The urinary stasis which predisposes to and perpetuates infection also favors the formation of stone which occurs in 4 to 5 per cent of these cases.

Chronic pyuria is the usual indication for the urologic examination which discloses the ureterocele and associated disease such as calculus and, notably, other urogenital tract maldevelopments.

Pain along the urinary tract or referred to the abdomen most commonly reflects the ureteropelvic back pressure engendered by the ureterocele obstruction. Yet vesical irritability with disturbances of urination is present in three-fourths of the cases.

The diagnosis is readily made by cystoscopy. Excretory urography may give the initial diagnostic clue when the ureterocele is demonstrated (1) positively as a bulbous intravesical cystic mass, or (2) negatively when outlined as a globular filling defect.

Ureterocele through its complications may be fatal.

Treatment demands prompt removal of the obstructive factor. The methods of accom-

plishing this have been described; transurethral electroresection of the ureterocele is relatively easy to perform and generally satisfactory. Ureteronephrectomy or ureterohemi-nephrectomy is sometimes demanded. Removal of complicating calculi and associated urosurgical conditions is often an essential part of the therapeutic problem.

Even though a satisfactory surgical result has been achieved by any of the various methods described and according to indication, no patient should be considered cured in whom sterilization of the urine is not accomplished.

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THE CANCER DETECTION CENTER

Its Effectiveness and its Role in the Control of Cancer, as Determined by a Follow-up Study of 1,000 Patients

EUGENE E. CLIFFTON, M.D., and BENJAMIN RUSH, JR., M.D., New Haven, Connecticut

IN any discussion of cancer detection centers a definition of terms is important. These facilities have had many designations including: Cancer Prevention Clinics, Cancer Detection Centers, Cancer Control Clinics, and Health Maintenance Cancer Prevention Clinics. They may best be defined in terms of their primary function, the discovery of early cancer in asymptomatic patients. While this definition seems clear, there is considerable variation in the actual operation of cancer detection centers throughout the country. Some centers attempt to restrict those examined to asymptomatic patients only, while others accept patients regardless of symptomatology. Some clinics offer a set, routine examination, and the patient is referred to his physician for any further procedures indicated. Other clinics offer complete diagnostic facilities.

In the 14 years since the first permanent Cancer Detection Center was established (13) the pendulum of medical opinion concerning these clinics has oscillated considerably, while tumor clinics, initiated some 7 years earlier under the auspices of the American College of Surgeons, are thriving and now are a fully accepted part of the medical program (8). Initial reports of the results of detection clinic operations were favorable (13, 14, 15), methods of organization and minimum standards were suggested (20), and in 1946 the National Advisory Cancer Council recommended cancer detection clinics as one of the basic elements of a cancer program (16). This opinion has not been accepted by many physicians (1, 10, 11). In California 4 cancer detection clinics were set up as pilot centers and 3 were subsequently discontinued (11). The chief criticisms of the clinics have been: (1) the difficulty in restricting the clinics to asymptomatic patients; (2) the low percentage of detections, estimated as low as 1 in 1,000 by some; (3) the high cost per detection; and (4) the large number of patients who do not receive diagnostic procedures recommended when they are referred back to their local physicians.

The New Haven Cancer Detection Center was established in 1947, under the auspices of Yale University School of Medicine and the Connecticut Cancer Society. It is conducted in, and uses most of the facilities of, the New Haven Tumor Clinic which began operation in 1929. To date more than 3,000 examinations have been conducted in the Detection Clinic. In 1950, three years after the opening of the clinic, a follow-up study of the results, including both successes and failures, was started. The study was set up so as to supply the following information: (1) the number of malignant tumors diagnosed, (2) the number of asymptomatic malignant tumors diagnosed (detections), (3) the number of malignant tumors in whom the diagnosis was missed, (4) the number of tumors developing in the follow-up period, and (5) methods of improving the performance of this clinic, and of the detection of tumors in general.

It was felt that this study should include a follow-up of all patients for a period sufficient to determine if any cases of cancer were missed in the routine examination (No. 3 above), if any patients failed to receive proper treatment when cancer was diagnosed,

From the Department of Surgery (Oncology) Yale University School of Medicine. Partially supported by the Anna Fuller Fund.

From the Detection Clinic, Tumor Clinic, and Tumor Registry of Yale University School of Medicine, supported by the Connecticut Cancer Society Fund No. 222, and the Jane Coffin Childs Fund No. 23-2. The special Follow-up Clinic was supported by funds from the Damon Runyon Fund for Cancer Research, Institutional Research Grants Nos. 34 and 86.

TABLE I.—AGE DISTRIBUTION

Age Years	No. of patients	Per cent with cancer
0–29	111	1.80
30–39	288	3.50
40–49	292	3.08
50–59	183	11.50
60–69	85	16.50
70–79	37	40.50
80–89	10	80.00

and what methods of examination provided the best returns in cancer diagnosis.

MATERIALS AND METHODS OF STUDY

The cases studied in this report were obtained from the files of the Yale University Tumor Registry[1]. A report on the first 790 patients seen in the Detection Clinic with follow-up studies in 91.3 per cent has already been made (6). The present study includes the succeeding 1,000 cases with complete follow-up in 97.7 per cent.

The routine examination at this clinic includes a complete history and physical examination, complete blood count, urinalysis, stool guaiac, photoroentgen of the chest, Papanicolaou smears of the cervix, and Mazzini. Auxiliary services include facilities for further diagnostic x-ray, endoscopic examinations, and facilities for biopsy as indicated.

This clinic differs from most other detection clinics in the following points: in each case an attempt was made to reach a final diagnosis before the patient was returned to his private physician; i.e., if a gastrointestinal series or biopsy was indicated, it was done at the clinic; if possible, the patient was referred back to his physician with a final diagnosis and suggestions for treatment; patients of every age group were accepted; no attempt was made to separate asymptomatic from symptomatic patients; and any patient applying for examination was accepted. Furthermore, most of the patients referred to the Tumor Clinic as proved or suspected cancer cases were submitted to the regular Detection Clinic examination. Cancers discovered in these patients were, of course, not considered detections unless they were completely unrelated to the lesion for which the patient was referred, and completely asymptomatic.

TABLE II.—SOURCE OF REFERRAL

Source	Per cent referred	Per cent with cancer
Self-referred	60.6	1.3
Cancer Information Center	25.2	1.2
Medical source	14.2	36.6

[1]Supported by the Jane Coffin Childs Fund for Cancer Research.

These 1,000 patients were seen consecutively between April 14, 1948, and September 16, 1949. The average age was 55.6 years with the age distribution shown in Table I. As may be seen, the age of the great majority were between the years of 30 and 60. Sixty-six per cent of the patients were females and 34 per cent were males. The patients were referred to the clinic by local physicians, by the local Cancer Information Center, and by self-referral. The distribution of the various sources of referral is shown in Table II.

In the follow-up an attempt was made to see the patient in the hospital clinics or to obtain the information through the patient's local physician. If this ideal could not be achieved, the information was taken as a statement from the patient over the telephone to a doctor at the hospital. In a few cases it was necessary to rely on a statement from the patient by letter. The distribution of sources of follow-up information is shown in Table III. The minimum follow-up was 12 months. Any patients followed for a shorter period than 12 months were considered as lost to follow-up. The majority of patients were followed for a much longer period, with the average length of follow-up being 22.6 months. The longest period any patient was followed was 40 months.

RESULTS

A diagnosis of cancer was made in 63 patients. Of these, 51 were referred by doctors because of suspected carcinoma. These were obviously not detections.

In the 12 remaining patients of this group a preliminary and final diagnosis of cancer was made in the clinic. The 12 patients were divided into 4 groups on the basis of the factors which led to the final diagnosis: group I, patients with a chief complaint which led directly to the diagnosis of a cancer; group II, patients without a pertinent chief complaint but in whom, in the system review of the his-

tory, symptoms were revealed which led to the diagnosis; group III, patients without a pertinent chief complaint and without significant complaint on system review, in whom the diagnosis was made on the basis of physical findings; group IV, patients without significant chief complaint, symptoms, or physical findings in whom the detection and diagnosis were made by laboratory methods. These groups, with the sites of the tumors found and the factors leading to the diagnosis, are shown in Table IV. Groups III and IV can be considered true detections since the patients were completely without symptoms related to the lesion. Seven such true detections were made, an incidence of 0.7 per cent.

Four hundred and sixty-eight patients had chief complaints when they came to the clinic. Of these, 6 or 1.3 per cent were found to have cancer. Five hundred and thirty-two patients had no chief complaints when they came to the clinic. Of these, 6 or 1.1 per cent were found to have cancer. In this second group, 3 patients or 0.5 per cent were found to have cancer on the basis of laboratory tests alone.

Of the 977 patients who were followed for a year or more after being examined in this clinic, 16 (1.7 per cent) developed pathologically proved malignant tumors. A breakdown of this group with the sites of malignant tumor and the time following examination that the first symptoms of the tumor developed is shown in Table V. Six of these patients, the cases marked with asterisks in Table V, had lesions when they were examined which the clinic recommended should be followed by the patients' local physicians. Three patients had chronic cystic mastitis. One patient had intermittent vaginal spotting on an unexplained basis. One patient had had a carcinoma of the breast removed 10 years previously, and the last patient was a male with a hyperkeratotic lesion of the face.

Symptoms of tumor developed within 6 months of examination. If symptoms—which were eventually proved to be due to malignant tumor—developed within 6 months after the time the patient was seen in this clinic, it was considered that the tumor was present when the patient was examined and that the diagnosis was missed. A glance at Table V will show that only 2 patients are in this group. Their cases are given in brief as follows:

TABLE III.—SOURCE OF INFORMATION IN PATIENTS FOLLOWED

	Per cent
Hospital clinics	66.4
Telephone	18.6
Local physician	6.6
Patient's letter	6.1
None	2.3
	100.0

CASE 1013. A 53 year old white female came to the clinic with the chief complaint of a lump below the right shoulder blade. The history and system review were negative except for occasional headaches. Physical examination revealed a lipoma of the back, hypertension, a rectocele and cystocele, and chronic cervicitis. No adnexal masses were felt. The cervical smear was negative. The patient was discharged back to her local physician. One month after her examination here she began to complain of a feeling of pressure in the left lower quadrant and of backache. She was seen by her local physician who advised hot douches and baths. The symptoms became more severe and 8 months after her visit to the Detection Clinic a pelvic examination re-

TABLE IV.—TUMORS FOUND IN DETECTION CLINIC PATIENTS

	Site	Factor leading to diagnosis	Extent of tumor on treatment
Group I	Breast	C.C.* of lump in breast	Local
	Stomach	C.C. of fullness and belching with eating	Refused treatment
	Skin	C.C. of sore under eye	Local
	Salivary gland	C.C. of lump in neck	Local
Group II	Stomach	R.S.** occasional abdominal distress	Local
Group III	Skin	P.E.*** lump on arm	Local
	Meninges	P.E. hyperostosis of frontal sinus	Local
	Tongue	P.E. lump on tongue	Local
	Skin	P.E. lump on finger	Local
Group IV	Cervix	Papanicolaou smear	Local
	Cervix	Papanicolaou smear	Local
	Lung	Photoroentgen chest	Lymph nodes

The definitions for the groups are as follows: group I, chief complaint led directly to diagnosis; group II, patients without a pertinent chief complaint, but in whom symptoms were revealed in the system review of the history which led to the diagnosis; group III, patients without a pertinent chief complaint and without significant complaint on system review, in whom the diagnosis was made on the basis of physical findings; group IV, patients without significant chief complaint, symptoms, or physical findings, in whom the detection and diagnosis were made by laboratory methods. *C.C. refers to chief complaint; **R.S. refers to review of systems; ***P.E. refers to physical examination.

vealed a pelvic mass, thought to be a uterine fibroid. The patient came to operation at which time a large adenocarcinoma of the right ovary with peritoneal implants was found. The patient died 1 year later with extensive spread of her malignant disease.

CASE 1472. A 38 year old white female came to the clinic without a chief complaint other than the desire for a general check-up. However, in her system review she complained of infertility and menstrual irregularity of 2 years' duration with occasional intermenstrual spotting. Physical examination and laboratory examination including Papanicolaou smears were negative. Because of her menstrual history, the patient was referred to a gynecologist who followed her case for a period of 6 months. At the end of this time an enlargement of the uterus was noted and the patient was operated upon. A grade I adenocarcinoma of the fundus, confined to the endometrium, was found. The patient is now living and well without evidence of recurrence.

The first case cited is considered a misdiagnosis since it is likely that the lesion was present at the time the patient was seen in the clinic. It is unlikely, however, that the lesion was of a size that could be diagnosed by any methods now available. The second case is not considered a misdiagnosis since the possibility of a malignant lesion was suspected, and, because of the direct effort of the clinic, the patient was placed in the hands of a gynecologist who followed the patient and eventually removed the lesion at an early stage of growth.

Symptoms of tumor developed from 6 months to 2 years after examination. In the second 6 months after their Detection Clinic examinations, 5 patients developed symptoms which were later proved to be due to a malignant tumor. In the second year following their examinations, 9 patients developed the symptoms of cancer, later proved by biopsy. It is entirely possible that there were more cases of cancer during this period, since the follow-up was not complete in all patients during the second year.

Of the total of 79 proved cases of cancer (63 seen in the Detection Clinic plus 16 found in follow-up) 2 patients had previous histories of malignancy, an incidence of 2.6 per cent. These two diagnoses were: a bronchiogenic carcinoma of the lung found in a patient referred to the clinic with a carcinoma of the larynx, and an adenocarcinoma of the left breast in a woman who had had a radical mastectomy for a malignant tumor in the right breast 10 years previously.

Of the 12 patients in whom carcinoma was discovered in the Detection Clinic, 2 have died. One patient with carcinoma of the stomach refused treatment; the other with carcinoma of the lung was found to have metastatic disease at operation and died postoperatively. The remaining 10 patients were speedily treated. Their neoplasms were found to be localized at operation, and they are living and well without evidence of recurrence at present. Of the 16 patients who developed carcinoma at some time during the follow-up period, 9 (56 per cent) had localized lesions at the time of treatment and are living and well without recurrence at present. Seven (44 per cent) of the 16 patients had metastatic spread of varying degree at the time of treatment. Two of these are now dead. The remainder are living and well without symptoms of recurrence.

Of the total number of patients seen, 73 were discharged with a frank diagnosis of psychoneurosis. Most of these cases were neuroses of a minor nature rather than psychoses.

To summarize the results briefly, excluding those patients referred for suspected malignant tumors, the clinical and final diagnosis of malignancy was made in 12 or 1.2 per cent of 1,000 patients seen in the Detection Clinic. Cancers were diagnosed in 6 or 1.1 per cent of the 532 asymptomatic patients, and in 6 or 1.3 per cent of the 468 symptomatic patients. In patients with known cancers 2.6 per cent were found to have a second malignant tumor. Of the 977 patients followed after their examinations, 7 or 0.7 per cent developed cancer in the first year after examination. Of 389 patients followed for 2 years, 9 or 2.3 per cent developed cancer in the second year after examination. Of 14 patients who presumably had cancer at the time of the initial examination, 12 were immediately diagnosed correctly, 1 was suspected and followed with an eventual diagnosis being made, and in 1 case the diagnosis was missed; a ratio of 92.8 per cent correct diagnoses. Of

these 14, 2 or 14 per cent had metastatic lesions at operation. Of the 16 patients who developed carcinoma after being examined in the clinic, 7 or 44 per cent had metastatic lesions at operation. It is of interest that none of the asymptomatic patients discovered to have cancer refused treatment.

DISCUSSION

It can be concluded from these results that a detection clinic making full use of diagnostic facilities will yield approximately 1 case of cancer for every hundred patients examined in a mixed group of symptomatic and asymptomatic patients. It is interesting to note that in this series essentially the same ratio of cancers was found in asymptomatic as in symptomatic patients. The symptomatic patients seen in our clinic, other than those referred by physicians for the confirmation of suspected carcinoma, tend to be patients with vague and nonspecific complaints which have led them to request a general check-up. On the other hand, there is a definite group of patients who have had persistent symptoms of a misleading nature which have resulted in repeated misdiagnosis elsewhere. For this reason we feel that it is undesirable to attempt to restrict the clinic to asymptomatic patients alone. Moreover, as Garland has pointed out, such a restriction is difficult to enforce.

A true detection is here defined as the diagnosis by physical signs or laboratory methods of a neoplasm in a patient who is completely without symptoms referable to the lesion. Seven true detections (0.7 per cent) were made in this series. This is in relative agreement with a previous study of 790 patients from this center in which 5 (0.6 per cent) true detections were made (6). It is difficult to compare these results with other figures in the literature, since most reports have not made it clear what exactly constituted a detection. L'Esperance (14) has reported an incidence of 1½ per cent cancers in asymptomatic patients. The American Cancer Society (17) reported a yield of 0.8 per cent cancers and 10 per cent precancerous lesions in a mixed group of 51,728 symptomatic and asymptomatic patients seen in detection centers throughout the country.

TABLE V.—CANCERS DEVELOPING IN DETECTION CLINIC PATIENTS IN A 2 YEAR PERIOD FOLLOWING EXAMINATION

Site	Time, examination to 1st symptom (mo.)	Time, examination to definitive treatment (mo.)	Extent lesion at treatment
Ovary	0	8½	Peritoneal implants
Uterus (fundus)*	1	6	Local
Breast*	6½	9½	Lymph nodes
Stomach	8	14	Omental fat
Breast	9	9½	Local
Skin*	9	9	Local
Breast	11	17	Lymph nodes
Ovary	12½	19	Peritoneal implants
Colon	12½	15	Lymph nodes
Skin*	13	13	Local
Breast	15	19	Local
Breast	16	20	Lymph nodes
Breast*	16	17	Local
Breast	16	18	Local
Breast	19	19	Local
Breast*	21	21	Local

The time following Detection Clinic examination that these patients first noticed symptoms of a developing cancer is noted in the second column. The period between the first symptom and definitive treatment is calculated by subtracting the number of months noted in the 2nd column from the number of months noted in the 3rd column. The asterisks indicate patients who were advised by the clinic to be followed by their local physicians.

The 7 patients in whom silent cancers were diagnosed benefited greatly by the early diagnosis, since, of these 7, only 1 had metastatic spread of the cancer at operation.

A frequent criticism of cancer detection centers is the high cost per detection. This figure has been estimated to be as high as 25,000 dollars per detection on a theoretical basis (10). This estimate is far above actual cost. Still, the cost per detection is high, probably ranging from 1,000 to 3,000 dollars. On the other hand, this is an impractical and rather arbitrary index of the services rendered by the detection centers. In addition to cancer detection per se, the clinics play an important public health role. Detection centers report that 50 per cent or more of their patients are referred to local physicians for the treatment of nonmalignant lesions (14, 15). Schram has referred to these centers as "Health Maintenance" Cancer Detection Centers, and this seems an accurate definition of

their function. Another important benefit derived from the centers is the education of the patients in the detection of cancers in themselves. It will be noted that of the 9 women who developed cancer of the breast after being seen in this clinic, 6 or 67 per cent reported to their physicians and had radical mastectomies performed while the disease was still localized; 33 per cent had lymph node involvement at the time of operation. This is a complete reversal of the usual statistics, since at present the majority of women with carcinoma of the breast have lymph node involvement at operation (1, 7).

A third benefit of the cancer detection center is the opportunity to train men in the proper methods for the detection of cancer as well as the evaluation of new techniques for cancer detection; these last are most feasible in centers attached to teaching hospitals (23).

Finally, the cancer detection center should set a standard for the detection of cancer in the community. The doctor's office is, and probably always will be, the major center for cancer detection. The detection center's role should be to set the pattern for detection, evaluate the best methods to follow, and offer instruction in these methods to interested physicians.

What can the detection centers do to increase the yield of detections? There are several approaches to this problem. One of the simplest methods would be to restrict the group examined to the older age groups. As can be seen in Table I, the lowest number of malignant lesions was found in patients under 30 years of age. In addition, the 2 neoplasms found in this age group were lymphomas and were little benefited by treatment. The policy of this clinic at present is to advise examination of women 35 years of age and over, and men 40 years of age and over, although some younger patients are still accepted.

Patients who have had previous carcinomas are excellent candidates for detection clinic examinations, since the incidence of secondary carcinoma, unrelated to the first lesion, is even higher than in those patients without previous cancer.

The availability of complete diagnostic facilities to the detection center, so that a final diagnosis of cancer may be made before the patient is returned to the referring physician, is almost essential. Curphey has stated that as high as 50 per cent of patients referred back to their own doctors with recommendations for further diagnostic procedures never receive the recommended work. This was possibly due to negligence on the part of the patient, but frequently the physician was at fault. On the other hand, when a patient is returned to his physician with the definite diagnosis of cancer, there is usually little delay in bringing the patient to treatment.

New techniques of examination are being developed and may be of considerable value. Routine sigmoidoscopy has been evaluated in a number of centers and shows definite promise (4, 24). The examination of smears of various secretions, other than the cervical smear, is progressing. Smears of gastric aspirations for the detection of gastric carcinomas are being developed, but are just becoming practical (21). Smears of prostatic fluid for the detection of prostatic carcinoma may be of value (19). Another proposal which deserves serious consideration is the use of serological tests for cancer. Several of these tests are now available (5, 11, 18). They are nonspecific and at the best give positive reactions in but 75 per cent of all cancers. However, it is usually not realized that these tests are best in those instances in which the present methods of physical examination and history taking are least dependable; that is, in the detection of internal carcinomas. One such test reports positive results of 90 per cent or over in carcinomas of the lung, biliary tract, pancreas, and kidney (5). A test of this sort in conjunction with routine detection clinic examination should be of considerable value, the two methods being complimentary to each other.

As another approach toward increasing the yield of positive cancer diagnosis in a detection center, we should consider the possibility of shortening the length of the examination. Care must be taken not to sacrifice quality for quantity. It is doubtful if the physical examination could be shortened much even by restricting the areas examined to those in which cancer is most frequently found. Cer-

tainly the most care should be taken in examining the skin, mouth, breasts, lymph nodes, rectum, and cervix. The efficiency of history taking might be increased considerably by letting patients fill out a standard questionnaire such as the Cornell Medical Index (3). By looking over the completed questionnaire, the examining physician could easily pick out the systems in which special attention was needed.

With the advent and spread of cancer information centers, cancer detection centers, and the flourishing publicity directed to cancer in the past decade, the fear has frequently been expressed that considerable cancerophobia was being created. In this clinic 7.3 per cent of the patients seen received a diagnosis of psychoneurosis of a major or minor nature. It is unlikely that this figure is any higher, or even as high, as the number of psychoneurotics seen in the office of the average general practitioner daily. Jones and Cameron suggest that cancer publicity may cause neurotics to fix upon cancerophobia as an expression of their illness in place of some other disease, but does not cause normal patients to become cancerophobes. This opinion is confirmed by our attending psychiatrist (22), who has made a special study of this problem.

SUMMARY AND CONCLUSIONS

1. The effectiveness of the Cancer Detection Center examination at New Haven Hospital was evaluated by determining the number of true detections made in a series of 1,000 patients, and by determining the number of cancers missed by follow-up of the patients over a period of at least 12 months.

2. It was found that when the Detection Center was conducted in association with full diagnostic facilities and a proper follow-up system, the large majority of silent cancers were diagnosed.

3. The percentage of silent cancers detected in a group of patients as the result of a single examination of each patient may not be high enough to justify the cost of operation of a detection center, but other indirect benefits derived from detection centers in addition to the cancers detected do justify the continuation of detection centers in selected institutions.

4. These indirect benefits include especially the use of the detection centers for the evaluation of new methods of detection, the contribution made by the detection centers to the education of the medical and lay public concerning cancer detection, and, lastly, the benefits from early diagnosis of diseases other than cancer.

5. Methods for increasing the yield of cancer detections are discussed, and the use of one of the presently available nonspecific serological tests for cancer in conjunction with the routine cancer detection examination on an investigational basis is recommended.

6. Patients in whom silent cancers are diagnosed are greatly benefited by the early diagnosis, as indicated by the low incidence of metastatic lesions in these patients.

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SYMPATHECTOMY IN THE TREATMENT OF FROSTBITE

HARRIS B. SHUMACKER, JR., M.D., F.A.C.S., Indianapolis, Indiana

THERE is a great variety of opinion concerning the relative importance in frostbite and the related cold thermal injuries of damage due to cold itself on the one hand and of injury and dysfunction resulting from circulatory alterations consequent to the exposure on the other. In spite of these differences in opinion, however, it is perfectly clear that there are pronounced changes in the local circulation from the beginning of the exposure until full recovery has been achieved. Indeed altered vasomotor function not infrequently persists as a more or less permanent sequel to the injury. Since the vascular changes which occur during and immediately after the exposure and after the period of inflammatory hyperemia are characteristically those of vasoconstriction and sympathetic overactivity, it would seem important to inquire into the possibility of modifying the natural course of events by sympathetic interruption. Furthermore, it is known from capillary microscopy (4) and arteriography (19) in experimental frostbite that the circulation to the injured part even during the period of so-called reactive hyperemia is not necessarily full and complete in spite of the local warmth.

Relatively few observations concerning sympathectomy in frostbite are recorded in the literature. There are a number of reports dealing with experiences gained from the use of sympathetic blocks early in the course of frostbite (2, 5, 6, 8, 15, 16, 20). One of them (6) includes, in addition, observations based upon 12 operative lumbar sympathectomies performed a number of days after frostbite. The benefit felt to result from this procedure led to the recommendation that sympathectomy be carried out in all cases which appear grave after the edematous phase. These experiences with sympathetic ganglionectomy and sympathetic blocks, as well as a few with periarterial sympathectomy and arterectomy, suggested to the authors that sympathetic interruption early after frostbite tends to bring about cessation of pain, rapid subsidence of edema, quicker demarcation of viable and gangrenous areas and a more active circulation with better granulations and quicker healing. In 1943, I reported experiences with sympathectomy performed at a later time following frostbite in 5 patients and at that time I felt that there was convincing evidence that this operation had a definite place in the treatment of such difficulties (17). During the same year Telford reported that he had used sympathectomy with gratifying results in the treatment of the late sequelae of frostbite in 4 patients.

Because of the limited observations recorded in the literature, I have thought that it might be helpful to analyze my experience with 33 sympathectomies performed in 20 patients. In all of them the injury resulted from exposure to more or less dry cold. In many there was a clear-cut history of actual freezing of the part; in others it seems doubtful that actual freezing took place. No cases of trenchfoot or immersion foot are included, my experiences with sympathectomy in trenchfoot having been reported previously (18).

In 2 patients sympathectomy was performed within the first week after freezing (Table I). One 41 year old man had a severe injury of the left foot and a mild injury of the right. Gangrene of all the left toes was evident as well as of a large area under the head of the first metatarsal and of a small area on the heel. The foot was hot while the toes were cold and blue. The pulses were bounding and oscillometric values were increased as compared with those of the right lower extremity which appeared perfectly normal 7 days after injury at the time the left lumbar sympathectomy was carried out. The left foot and distal half of the leg were markedly edematous and

From the Department of Surgery, the Indiana University Medical Center, Indianapolis, Indiana. Aided by a contract between the Office of Naval Research, Department of the Navy, and Indiana University.

TABLE I.—SYMPATHECTOMY IN THE EARLY TREATMENT OF FROSTBITE

Case No.	Age of patient years	Interval in days between injury and sympathectomy	Symptoms and signs before operation	Extremity sympathectomized	Result of operation
1	41	7	Gangrene of all toes, of a large area under head of 1st metatarsal, of small area on heel. Marked edema. Anesthesia of toes, hypesthesia of sole. Moderate spontaneous pain. Foot hot, toes cold. Oscillometric values increased	L.L.	Pain disappeared. Edema quickly reduced. Rapid demarcation; well demarcated 4 days P.O. Toe amputations 17 days P.O. Skin grafts to ulcers 3 weeks later. Healing. Period in hospital: 56 days
2	20	5	Marked edema. Spontaneous pain. Sensitivity to touch. Apparent gangrene toes and distal foot. Foot hot, pulses full	R.L. L.L.	Pain disappeared. Edema quickly subsided. Gangrenous plaques rapidly demarcated. Débridement. Healing. Period in hospital: 57 days

there were many vesicles, especially on the toes. The sole was hypesthetic and the toes were anesthetic. There was moderate spontaneous pain. Following sympathectomy the pain ceased. The edema rapidly decreased and shortly disappeared. There was a quick demarcation of the gangrenous areas; they were well demarcated on the fourth day after operation. The toes were amputated through the proximal phalanges 17 days after sympathectomy and 3 weeks later the denuded areas were covered with skin grafts. After a total stay of 56 days, the patient left the hospital with the wounds healed.

The second patient was admitted to the hospital 1 day following severe freezing of both feet. There was marked edema of the distal halves of both legs and both feet (Fig. 1a). The feet were hot and the pulses were quite full. Large vesicles were present, particularly on the toes which were cyanotic and looked as if they might in large part be developing gangrene. Other areas in the distal portion of the feet also looked as if they might become gangrenous. The feet were quite sensitive to touch and there was considerable spontaneous pain. During the first 24 hours of his admission he required 15 milligrams of morphine and 2 doses of 100 milligrams of demerol. On the evening of his second hospital day a lumbar sympathetic block was carried out with considerable temporary relief of the spontaneous pain and the sensitivity of his foot to touch. The patient was given 10 milligrams of rutin twice daily and this medication was continued for 5 weeks. On the day of admission he was given 300 milligrams of dicumarol but received no further anticoagulant therapy. The prothrombin time dropped to 37.5 per cent 48 hours later but by this time it had been decided to perform lumbar sympathectomy and to discontinue anticoagulant therapy. Vitamin K was then administered. A bilateral lumbar sympathectomy was carried out 4 days after his admission to the hospital and 5 days after his cold injury. The condition of his feet was much the same as on the day of admission. They were hot, sensitive to touch and markedly swollen. The spontaneous pain ceased abruptly after operation; the edema subsided with remarkable rapidity, and there was quick demarcation of the areas of gangrene which appeared much less extensive than had been previously anticipated. Except for ultimate loss of most of the toenails, damage was limited to areas of superficial gangrene on the toes and along the lateral aspects of the distal portions of both feet (Figure 1b). The gangrenous plaques were removed 2½ weeks after sympathectomy. The denuded areas epithelized satisfactorily and the patient left the hospital asymptomatic with both feet well healed (Figure 1c) after a total hospitalization period of 57 days.

In 10 additional patients sympathectomy was carried out from 2 to 11 months after injury (Table II). Twelve lumbar sympathectomies were performed, the procedure being carried out bilaterally in 3 patients and unilaterally in 6. A bilateral upper dorsal sympathectomy was performed in the tenth case. Gangrene of varying extent had been present in 7 of the 10 patients but healing had taken place in all but 3 at the time of operation. Healing proceeded rapidly in these 3 cases. The apparent beneficial influence of sympathetic denervation in the healing of ulcerated areas which remain as the result of gangrene

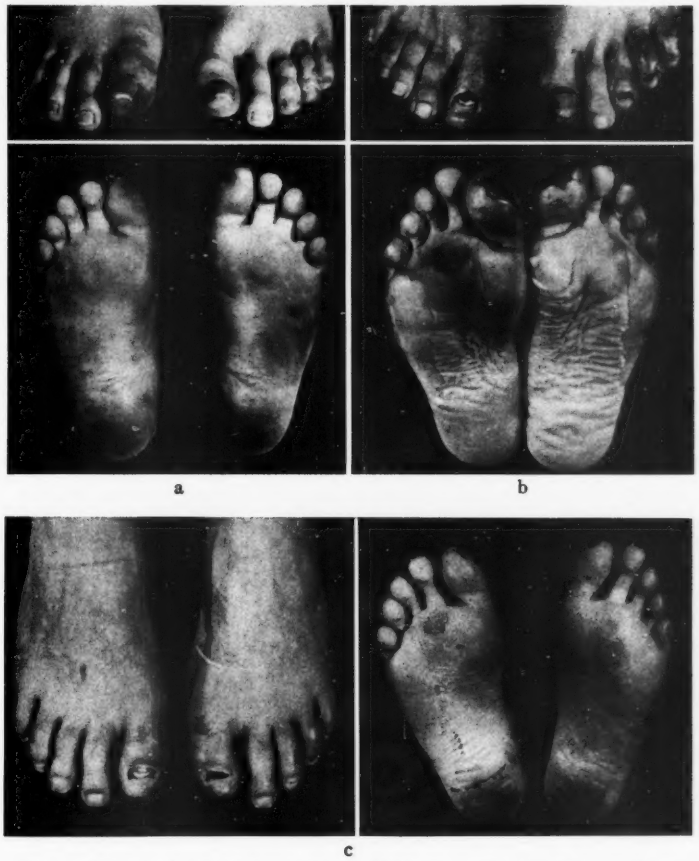

Fig. 1. Photographs of the feet in Case 2 (Table I). a, The condition on the day after admission. There was marked swelling of the feet. Unfortunately, the photographs do not show well the cyanosis and evidences of threatened gangrene. b, The condition 2 weeks after sympathectomy. The areas of gangrene of the toes and lateral surfaces of the feet are well demarcated. c, The condition a week before discharge from the hospital, 50 days after injury. The ulcerated areas remaining after débridement of the gangrenous plaques have healed.

is illustrated by the course of events in Case 9. This 12 year old child had sustained a severe freezing injury of both feet on February 2 when she walked barefooted from her home to an outside privy in a temperature of −15 degrees F. The following day she had been admitted to another hospital where she had remained for 3½ weeks. She was admitted to the Indiana University Medical Center on the 3rd of March, 1 month after her injury. At this time she had pneumonia, from which she quickly recovered. There were fairly large areas of superficial gangrene on both heels and both great toes (Fig. 2). Shortly after her admission to the hospital these gangrenous plaques were removed but the residual ulcers did not heal. Indeed 3 weeks later, at the time that bilateral sympathectomy was carried out, there was no evidence of any epithelization at all. The feet were sometimes warm but tended to be a little cool and to sweat excessively. Following lumbar sympathectomy they re-

TABLE II.—SYMPATHECTOMY IN THE INTERMEDIATE TREATMENT OF FROSTBITE

Case No.	Age of patient years	Interval in months between injury and sympathectomy	Extent of loss of tissue	Gangrene or ulcer at time of operation	Symptoms and signs before operation	Extremity sympathectomized	Result
1	19	10	$LT_{1,2}$ $RT_{2,4}$		Some coldness and hyperhidrosis. Severe cold sensitivity	L.L.	Excellent
2	24	6			Aching, burning, coldness, cyanosis, severe cold sensitivity	L.L. R.L.	Excellent
3	30	11	LT_2 complete		Slight tingling, burning pain on standing. Moderate cold sensitivity	L.L.	Excellent
4	21	6	All toes, worse right	RT_4	Burning, hyperhidrosis. Moderate cold sensitivity	R.L.	Good
5	23	5	$LT_{1,2,3,4}$		Cyanosis, coldness, moderate cold sensitivity	L.L.	Excellent
6	21	11	$LT_{1,2,3}$		Coldness, cyanosis, moderate cold sensitivity	R.L.	Excellent
7	21	5			Coldness, cyanosis, hyperhidrosis, soreness of heel on standing, numbness at heel. Moderate cold sensitivity	L.L. R.L.	Excellent
8	20	10	RT_1	RT_1 .	Burning pain, moderate cold sensitivity	R.L.	Good. Pain almost all gone
9	12	2	RT_1 heel LT_1 heel	RT_1 heel LT_1 heel	Coldness, hyperhidrosis	L.L. R.L.	Excellent. Ulcers healed
10	45	2½			Numbness, coldness, pain. Moderate cold sensitivity	R.U. L.U.	Excellent

mained warm and dry and epithelization was so rapid that complete healing took place before her discharge on the fourteenth postoperative day. In 1 of the cases amputation of a gangrenous toe was necessary (Case 8). Healing was rapid but there was a small ulcer still present when the patient insisted upon leaving the hospital. He remained ambulatory, neglected the foot in general, and in this instance a tiny ulcer remained unhealed for a long time. It is noteworthy that freezing in this case had been followed by extensive thrombosis of arteries in the foot which, even though its circulation was improved somewhat by sympathectomy, nevertheless remained rather cold and had obviously impaired circulation.

All of the patients showed evidence of vasoconstriction and sympathetic overactivity even in an ordinary warm environment. In some, however, such changes were mild. In most of them there was evident coldness of the feet and in quite a few definite hyperhidrosis and cyanosis. Four patients complained of rest pain even in a warm environment, and in 3 of the 4 the pain was distinctly burning in character. An additional patient complained of burning pain and tingling of the feet on standing while another complained of soreness of his heels when he stood. These symptoms were all relieved after sympathetic denervation except for persistence of very mild pain in the 1 patient, previously mentioned, who left the hospital before healing of a small ulcerated area had taken place. The feet or hands were warm, dry, and comfortable. The numbness present in the heel in Case 7 and in the finger in Case 10 disappeared after operation.

In 9 of the patients there was definite sensitivity of the affected part to cold while in the exceptional patient, Case 9, exposure to a cold environment was not carried out and it is not known whether cold sensitivity existed. When the patients were placed in a cold environment they complained of coldness, sometimes of numbness, and of various types of pain in the affected part, usually stinging, pricking, and burning. In all patients with sensitivity to cold, except Case 10, the patient's ability to withstand cold was carefully tested after operation either by subjecting him to cold temperatures out of doors or by placing him with the affected limb bare in a room maintained at 4 or 5 degrees C. For all practical purposes complete relief of such symptoms followed operation in all patients. In Case 4 there did remain very slight burning upon exposure to

severe cold. The others could withstand exposure to cold extraordinarily well.

Six patients were treated by bilateral lumbar sympathectomy and 2 by bilateral upper dorsal sympathectomy for late sequelae of frostbite (Table III). Treatment was carried out from 3 to 22 years after the injury. Four of the patients were under 40 and 4 were over 50 years old at the time of operation. Five of the patients had complaints which seemed largely vasospastic in nature. One young lady (Case 5) who had never had any circulatory difficulty before developed a syndrome indistinguishable from true idiopathic Raynaud's disease within a few weeks after a mild frostbite of both hands. The disorder became progressively worse and 3 years later she developed rapidly a very severe sclerodactylia. The attacks of vasospasm ceased after sympathectomy and there was increased mobility of the fingers. Another young woman (Case 3) developed vasospastic attacks much like Raynaud's associated with burning pain. She experienced complete relief after sympathectomy. Still another young woman (Case 4) developed marked vasospasm of both feet and legs after a mild frostbite, with coldness, cyanosis, hyperhidrosis, and slight edema, and with peculiar purpuric manifestations limited to the area of vasospasm. All these changes were worse upon exposure to cold. The vasospastic phenomena were relieved by operation and the purpura could be controlled well with elastic support. One 31 year old man (Case 7) who had sustained frostbite of both feet at 16, had coldness, cyanosis, hyperhidrosis and edema, as well as throbbing and aching on standing or walking. Of these complaints only slight aching of the feet on walking remained after sympathectomy. The result in Case 8 cannot yet be fully evaluated. Sixteen years before he had sustained severe frostbite of both hands resulting in gangrene and loss of the ends of all the fingers. Each year in cold winter weather he would develop recurrent ulceration of the tips of the stumps and each year more tissue would be lost. Finally only parts of the proximal phalanges remained. The stumps had been débrided and were healing slowly before sympathectomy was carried out. Healing progressed nicely afterward and

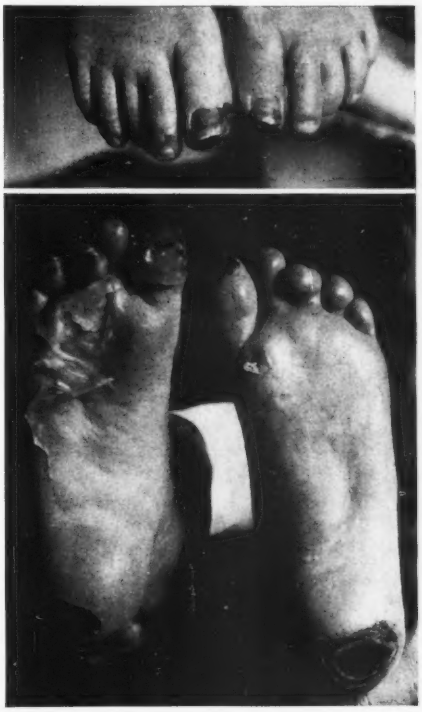

Fig. 2. Photographs showing the feet in Case 9 (Table II). The areas of gangrene of both heels and great toes involve the full thickness of skin and the residual ulcers after débridement were approximately the same size as the gangrenous plaques. No epithelization took place during the 3 weeks between débridement and sympathectomy. Healing proceeded rapidly after sympathectomy.

was soon complete. Since he has not yet passed through another cold season it remains to be seen whether or not sympathetic denervation will prevent recurrence of ulceration. In none of these 5 patients was there any evidence of obliterative changes in the arteries.

In the remaining 3 cases (Cases 1, 2, and 6) there was evidence of occlusion of arteries in the feet. Two had had recurrent ulcers of toes and in 1 of them parts of nearly all the toes had gradually been lost over a period of years. In all 3 the feet tended to stay cold and 1 patient had numbness and pain in the feet as well as coldness. Improvement followed operation in all. The ulcers healed. The pain present in the 1 patient was relieved except for some residual soreness of the heels. Varying

TABLE III.—SYMPATHECTOMY IN THE LATE TREATMENT OF FROSTBITE

Case No.	Age of patient years	Interval in years between injury and operation	Symptoms and signs before operation	Extremity sympathectomized	Result
1	55	22	Coldness and recurrent ulceration, with gradual loss of parts of nearly all toes. Ulcer left foot at time	L.L. R.L.	Good. Ulcer healed promptly. Circulation improved slightly
2	55	Years	Coldness, numbness, pain in feet	L.L. R.L.	Excellent. All symptoms relieved except for incomplete relief of soreness of heels
3	38	3	Raynaud-like attacks of vasospasm with burning pain	L.L. R.L.	Excellent. Complete relief
4	24	7	Legs and feet cold, cyanotic, hyperhidrotic, slightly edematous. Worse on exposure to cold. Purpura legs and feet	L.L. R.L.	Good. Vasospasm relieved. Purpura well controlled with elastic support
5	26	3	Raynaud's attacks, severe. Marked sclerodactylia	L.U. R.U.	Good. Attacks ceased. Sclerodactylia improved
6	64	12	Chronic and recurrent ulcers of toes. Hammer toes. Coldness	L.L. R.L.	Good. Ulcers healed. Circulation much improved in right, slightly in left foot
7	31	15	Coldness, cyanosis, hyperhidrosis, edema. Throbbing and aching on standing or walking	L.L. R.L.	Good. Symptoms relieved except for slight aching in feet on walking
8	52	16	Recurrent ulcers all fingers each winter with gradual loss of digits	L.U. R.U.	Unknown. Ulcers continued to heal but has not yet passed through another winter season

degrees of improvement in circulation were noted. In Case 1 only slight improvement in circulation was evident though the ulcers healed promptly after operation. In Case 6 there was marked improvement in the right but only slight improvement in the more severely affected left foot. In Case 2 marked improvement followed sympathectomy with disappearance of the coldness and numbness.

DISCUSSION

The role of sympathectomy in the intermediate treatment of frostbite as well as in the care of the late sequelae seems fairly clearly defined, although it will certainly be desirable to have our knowledge broadened by further experiences. The cases available for analysis are not numerous, to be sure, but the months or years of difficulty which have preceded sympathectomy serve in a sense as a valid control in each case for the alterations which take place afterward. The shorter the interval between injury and operation the more difficult is objective evaluation of the procedure, for it must be recognized that frostbite results in variable permanent damage and that it is difficult or impossible to estimate the eventual outcome in any patient shortly after injury. When a number of months have passed by, however, the situation is generally sufficiently well stabilized to permit one to judge objectively the results of treatment in any given patient.

In those relatively uncommon cases in which obliterative arterial changes have developed as a consequence of frostbite, the response to sympathectomy will depend, as in other sorts of obliterative arterial disease, upon the magnitude of associated vasospastic phenomena or upon the capacity of the vascular bed to undergo vasodilatation as the result of elimination of vasoconstrictor impulses.

The persistent vasospastic phenomena and associated symptoms which so commonly follow frostbite and the difficulties experienced upon exposure to cold are generally relieved entirely or almost completely by operation. It would seem, furthermore, that when annoying symptoms of increased vasomotor activity or bothersome sensitivity to cold persist for a number of months they are unlikely to disappear spontaneously. The increased circulation resulting from sympathectomy appears definitely to facilitate the healing of ulcers. Having treated a number of patients whose periods of hospitalization were prolonged many months because of slow-to-heal ulcers which have remained after débridement of areas of gangrene or amputation of toes, I cannot help wondering whether the periods of

hospitalization could not have been shortened greatly and better end results obtained had sympathectomy been employed in some of them relatively soon after injury.

Sympathectomy as a measure to be applied in the intermediate phase of treatment of frostbite and in the treatment of its late sequelae does not differ essentially from the use of sympathectomy in similar stages of trench foot. There is, however, one important difference. Painful sequelae which apparently result from damage to small nerves or nerve endings and which seem unrelated to vasoconstriction or vasodilation follow trench foot much more commonly than frostbite. Hence a larger percentage of patients requiring sympathectomy for frostbite will experience complete relief than is the case with patients suffering from trench foot.

The use of sympathectomy and sympathetic blocks early in frostbite, within the first week after injury, obviously needs further clarification. The observations described in the literature are based principally upon experiences with sympathetic block. There are recorded only a small number of cases treated by sympathectomy and this report adds only a few additional observations. The great difficulty in properly evaluating the results of any method of treatment early in frostbite is recognized. The injury is too variable to permit one to estimate accurately what the outcome in any given case would be without any treatment at all. It is almost certainly significant, however, that almost all of the recorded observations are in essential agreement as to the apparent effect of sympathetic interruption—prompt relief of any pain or sensitivity that may be present, rapid subsidence of edema, quicker demarcation of gangrenous and viable parts, quicker healing of residual ulcers. It is also of interest that similar conclusions concerning the effect of sympathetic interruption have been reached in the few cases of apparently equal bilateral involvement in which only one limb has been treated leaving the other to serve in a sense as a control.

No clinical experiences with the use of sympathetic interruption as an immediate emergency measure in the treatment of frostbite are recorded in the literature. The results of sympathetic block, sympathectomy and employment of general vasodilating agents in the immediate treatment of experimental frostbite are variable (1, 3, 7, 9–14). It is of interest, however, that such measures have either not altered the outcome at all or have brought about a decrease in the incidence and extent of tissue loss. None of these experiments has shown such measures to be harmful. Carefully studied cases of human frostbite treated in this fashion are sorely needed.

CONCLUSIONS

Sympathectomy has a definite place in the intermediate and late treatment of frostbite and the related cold injuries. The few observations available for analysis suggest that it also may be a useful measure in the early treatment of certain cases, tending to bring about rapid disappearance of pain, sensitivity, and edema, quicker demarcation of gangrenous areas, and more speedy healing of residual ulcers. Additional careful observations are, however, needed in order to confirm these impressions and to delineate better the indications for its use.

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THE MEASUREMENT OF THE PULSATILE ARTERIAL CIRCULATION

CARL A. JOHNSON, M.D., Chicago, Illinois

THE purpose of this paper is to describe an oscillometer for making permanent, timed, calibrated recordings of the pulsatile arterial circulation in the head, neck, and extremities from birth to old age. This method has its greatest usefulness in experimental and clinical medicine, experimental and clinical surgery, and experimental physiology and pharmacology. The information obtained is useful for a better understanding of cardiovascular function, as a diagnostic aid in cardiovascular diseases, in following the progress of treatment, and in studying the action of various drugs upon the cardiovascular system.

Oscillometers and plethysmographs have been used since early times; the first of which any record can be found was designed and used by Jan Swammerdam (1637–1686) for the study of muscle physiology. Since then many plethysmographs and oscillometers have been made and used for various studies such as, oncometers for the study of slowly changing volumes or organs associated with congestion and decongestion with blood, the Henderson cardiometer for measuring rapidly changing volumes, and numerous present day instruments. The one which forms the basis of this paper belongs to the second group.

It is difficult to classify some of the modern instruments into one of the two types, namely as plethysmographs or oscillometers. In accordance with the dictionary definition (2), some of the instruments called plethysmographs might more aptly be classified as oscillometers and vice versa.

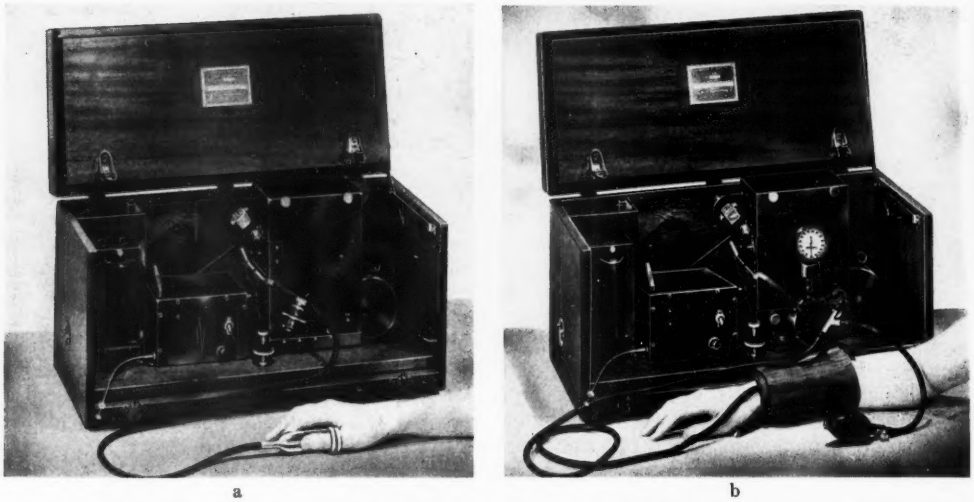
Since the present discussion is concerned with the measurement of the pulsatile arterial circulation, comments will be limited to a discussion of instruments used for this purpose. These devices measure volume changes electrically, photoelectrically, or mechanically. Some use electronic amplification, some use mechanical levers, and others optical levers for recording. However, some use no amplification such as the oscillometer to be described which actually uses a reduction of about 10:1. Of the mechanical instruments, air conduction is used by some, while others make use of some form of liquid for conduction of the pulse wave. The recordings are visual, photographically recorded, or recorded by writing levers.

From the Circulation Laboratory of St. Luke's Hospital and the Department of Clinical Science, University of Illinois College of Medicine, Chicago.

THE INSTRUMENT

The oscillometer to be described is an improved model of ones previously reported in which the registration of the pulsatile arterial circulation was limited to the fingers and toes (4, 5, 6). By means of an attachment, it is now possible to make arterial records from any part of the extremities, the neck, and the head. The instrument is illustrated by Figure 1 a and b and consists of three parts, the pickup, transmitting, and recording mechanisms (Fig. 1 b).

The pickup mechanism consists of a standard reinforced cuff for adults, and an infant's blood pressure cuff for infants and for records taken from the forehead, temporal area, or neck of adults. This is connected to the transmitting device which consists of an outer chamber connected to a blood pressure gauge and indirectly joined through a flexible metallic diaphragm to a second chamber. The second chamber is attached to a pipette calibrated to .01 cubic centimeter. When the "by-pass" stopcock is closed, the second chamber forms a closed system with a droplet of ethyl alcohol contained in the pipette, and acts as the recorder. The pipette is placed horizontally in front of a slit at such a distance that the droplet of alcohol, which acts as a lens, comes to focus on the sensitive paper and produces an intense black image on the developed paper.



a b

Fig. 1. a, This illustration shows the instrument and the manner of taking records from the fingers. Note that the transmitting device has been removed from the instrument. Note also that this instrument is an improved model of one previously described. b, This photograph illustrates the manner of taking records from the right wrist. Records taken elsewhere in the extremities are done in a similar fashion. The pickup mechanism (standard reinforced cuff) is shown attached to the wrist. This, in turn, is connected to the transmitting mechanism to which the blood pressure dial is attached. The pickup mechanism is inflated to any desired pressure which can be read directly from the aneroid blood pressure dial. The transmitting mechanism also acts as a reducer of the volume changes and in this particular instrument effects a reduction of about 10:1. The recording mechanism consists of a graduated glass tube containing a droplet of alcohol which in turn functions with a camera mechanism and timing mechanism to record the oscillations of the droplet of alcohol. Other features of the instrument are included in the text. The technical details of operating this instrument are contained in a small booklet which accompanies each instrument, or may be obtained by writing the manufacturer.

FEATURES OF THE OSCILLOMETER

For ease of operation and convenience of recording, the following features are incorporated into the design of the instrument:

1. It operates on 110 volts alternating current.

2. Illumination can be turned on or off independently of the camera mechanism. This allows for running blank strips of paper.

3. Standard 50 foot rolls of 6 centimeter daylight loading electrocardiograph paper are used.

4. An automatic electrical mechanism turns on a red light when the instrument requires a new roll of paper.

5. The camera and timer operate only when records are actually being taken. In use, this seems to be an improvement over the older model (6) which ran continuously and the paper was carried through by a clutch mechanism when desired.

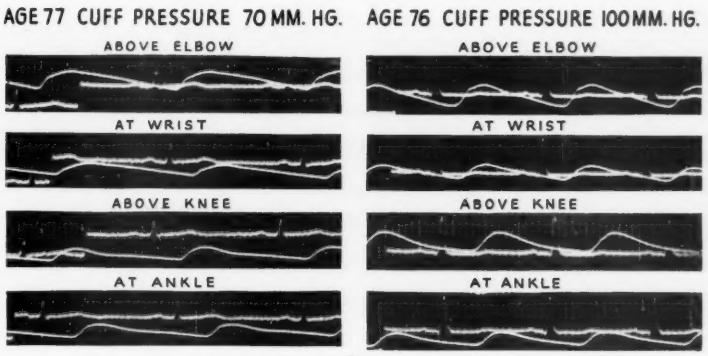
6. A lineage counter is incorporated. Only the desired length of record need be taken.

7. Exposed paper enters a removable lightproof container.

8. The optical system is such that the calibration lines on the recording pipette intercept the light rays and calibrate the paper with horizontal lines. The droplet of ethyl alcohol acts as a plus cylindrical lens which produces an intensely black image on the developed paper. A synchronous timer produces vertical lines with an interval of .04 second.

9. The instrument has 8 speeds of from 1.4 to 5.3 centimeters per second.

10. The amount of light is controlled by means of filters. By using the medium filter for the 4 faster speeds and the dark filter for the 4 slower speeds one can obtain about the same intensity of the image on the exposed developed paper.



b

Blood pressure	Normal Elbow Wrist 110/60	Normal Knee Ankle 120/80	Hypertension Elbow Wrist 154/92	Hypertension Knee Ankle 220/140
Time . . Peak of *R* wave to beginning of pulse wave	.14 .17	.19 .21	.12 .14	.17 .19
Difference in seconds	.03	.02	.02	.02
Distance in inches	11.25	11.75	10.75	13.00
Rate of pulse wave in feet per second	31.20	32.80	45.00	54.00

11. Satisfactory records can be obtained in a well lighted room.

12. Switches are spark-proof, thus the oscillometer can be safely used in the operating room.

13. The whole instrument is contained in a single portable unit.

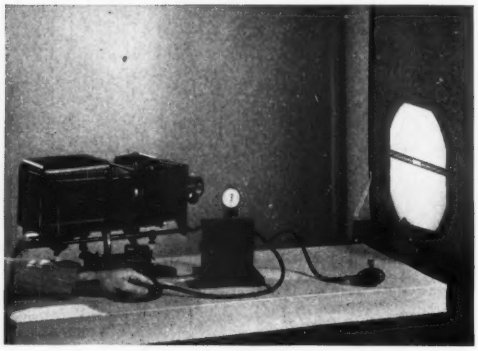
14. Any recorded pulse wave can be reproduced experimentally in every detail by a device used as a mechanical heart and constructed to calibrate and test the oscillometer.

a

Fig. 2. The equipment required to measure the speed of the pulse wave consists of a string galvanometer electrocardiograph with a fast speed and a pulse recorder, the transmitting device of the oscillometer, and the pickup device of the oscillometer. The procedure for measuring the speed of the pulse wave is as follows: a standard electrocardiogram is taken, the lead in which the *R* wave is most prominent is determined, and this acts as a point of reference. a, The transmitting device is attached to electrocardiograph and the pulse recorder, as shown in the photograph. b, A synchronous record is made of the electrocardiogram with the chosen lead and the pulse wave, using a cuff pressure at or about the diastolic pressure. These records are made above the elbow and at the wrist, and by means of a rule the distance between the applications of the cuff is determined. The distances in time from the peak of the *R* wave to the beginning of the pulse wave above the elbow and at the wrist are determined. The difference of these two figures represents the speed of the pulse wave in time, and knowing the distance one can compute the speed of the pulse wave in feet per second. Likewise, one can apply the same procedure in the other arm and in both legs. The illustration, b, shows how this procedure is carried out and how the computation is made.

USE OF THE INSTRUMENT

The instrument can be used for making recordings of the pulsatile arterial circulation from the following locations: fingers, large toes, above the elbow, at the wrist, above the knee, below the knee, ankles, insteps, the neck, over the temporal arteries, and in the presence of trephine holes of the skull from the brain tissue. These recordings can be made on subjects from birth to old age, and under certain conditions during birth, such as in a breach delivery, the pickup mechanism can be applied to the leg and recordings made during the course of delivery. The records reported in this study were all made on individuals at rest in the reclining position, but under special conditions such studies can be



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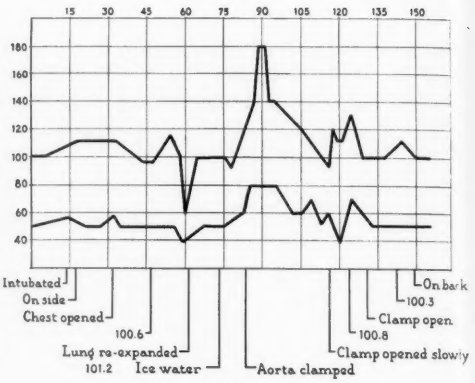


b

Fig. 3. a, This figure is self-explanatory and shows how the pulsatile arterial circulation is projected on the screen. This arrangement can be used for classroom demonstration as well as for other purposes, including the projection of the pulsatile arterial circulation during surgery to determine the status of the patient, as shown in b. b, The patient from whom this chart showing vascular changes during surgery was made was a 1 year old infant with tetralogy of Fallot in whom an embolus had already necessitated the amputation of one leg. A Potts-Smith operation was done at the Children's Memorial Hospital. The above recordings were made continuously from the left wrist during the surgery. The point on the blood pressure dial at which obliteration of the pulse took place was considered to be the systolic pressure, and the point of maximum excursion was considered to be the diastolic pressure. These two observations could be determined as often as every 15 seconds. Furthermore, by observing the projection of the pulse wave, changes are noted in rhythm which usually foreshadowed a fall in the blood pressure. The chart indicates a very marked fall in blood pressure at the point labeled "lung re-expanded," which was preceded by a marked change in rhythm. One striking change in the record is noted when the aorta was clamped, producing an artificial coarctation of the aorta, and this was followed by a very striking increase in both systolic and diastolic pressure which returned to the infant's normal pressure after release of the aortic clamp. The infant recovered following the surgery. This procedure might only be useful in a very limited number of patients, such as the one illustrated, but it may be useful to demonstrate to large groups the vascular changes which take place during surgery.

made during exercise, for example, those now in progress on athletes at the University of Illinois under the direction of Professor Cureton.

The above recordings can be projected on a screen for visual observation by use of an attachment as shown in Figure 3. This method is particularly useful for demonstration of the arterial circulation and for estimation of the blood pressure during surgery on infants.

The transmitting mechanism of the oscillometer can be used with the pulse recorder of the standard string electrocardiograph for making synchronous records of the pulse wave and electrocardiogram. By this procedure, it is possible to measure the speed of the arterial pulse wave.

MAKING THE RECORD OF THE PULSATILE ARTERIAL CIRCULATION

The manner in which recordings are made from the fingers (Fig. 1a) and toes has previously been described (4, 5, 6) and, since there is no essential change in the procedure with the new equipment, need not be repeated here.

Only a brief description of the procedure in taking records from the other locations will be given here, but a very detailed account of this procedure can be had from the manufacturer of the instrument.

The pickup mechanism (standard reinforced blood pressure cuff) is applied to the chosen locality, such as above the elbow, and is connected to the instrument. Recordings of the pulsatile arterial change are taken at intervals of 20 millimeters of mercury from a pressure of 20 millimeters of mercury above the systolic pressure to 20 millimeters of mercury below the diastolic pressure and the tracing is developed in the usual way.

The simplicity of the instrument and the ease with which these recordings can be made can be gauged by the time necessary to train a

technician. All of the technicians operating the instruments now in use have been trained at St. Luke's Hospital, Chicago, and the time required to learn has been less than 2 hours in all cases. However, greater proficiency is acquired with practice. The procedure requires no mechanical skill.

MEASUREMENT OF THE SPEED OF THE PULSE WAVE

The speed of the pulse wave as well as synchronous records with the electrocardiogram may be had when the transmitting device (Fig. 2) and the pickup mechanism are used in connection with the standard string electrocardiograph with a pulse recorder attachment. The procedure is briefly outlined as follows:

The pickup mechanism and the transmitting device are attached to the electrocardiograph and pulse recorder as shown in Figure 2. The electrodes are attached to the subject in the usual way except that the arm electrodes are placed higher on the arm to allow for pulse records to be taken from the wrist. A preliminary electrocardiogram is taken from which it is determined in which lead the *R* wave is most prominent, as the peak of the *R* wave is used as a point of reference. The diastolic pressure of the patient is taken. Using the diastolic pressure, pulse records and the electrocardiograms of the chosen lead are taken simultaneously from each of the following locations: above the elbows, at the wrists, above the knees, and at the ankles. The distance in inches between the application of the pickup mechanism is measured, for example, between the elbow and wrist. From the delay of the pulse record, such as that taken from the elbow and the wrist as determined from the record, and from the distance, one can compute the speed of the pulse wave between these two locations. Anyone wishing a more detailed description of the procedure can obtain a small booklet on the subject by writing the manufacturer.

PROJECTION OF PULSATILE ARTERIAL CHANGES

The projection of the pulsatile arterial changes is a useful procedure especially for classroom demonstration. During surgical operation it is valuable for obtaining close

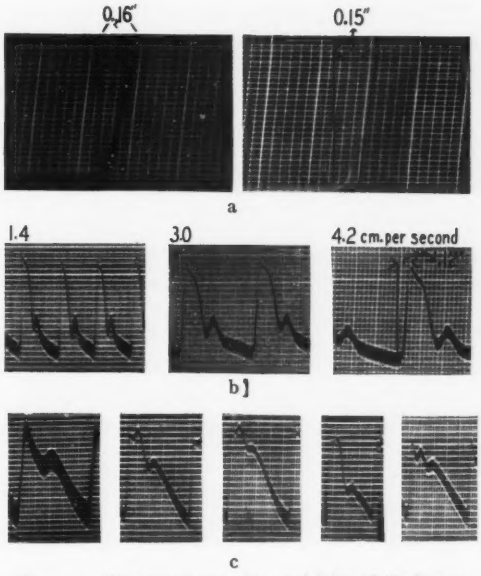


Fig. 4. a, To demonstrate the sensitivity of the instrument it was placed upon its side so that the pipette was vertical. The record on the left shows the falling of the droplet of ethyl alcohol in the glass tube under the force of gravity; on the right, a droplet of alcohol falling in front of the pipette. One notes that the times are approximately the same, indicating that the pipette offers no more resistance to a falling droplet of alcohol than the same droplet of alcohol falling in air. b, The difference in the appearance of the same pulse wave at different rates of recording. The instrument has a range of 1.4 to 5.3 centimeters per second. In this instance, illustrations are shown of the same pulse wave at 1.4, 3.0, and 4.2 centimeters per second. c, The pulse waves taken from different individuals to show that the position of the various notches and waves may vary. In the first illustration from the left the first notch is buried in the anacrotic limb. In the second, the first notch is on the anacrotic limb; in the third illustration, the first notch is at the peak; in the fourth illustration, the first notch is on the anacrotic limb; and in the fifth illustration, the first notch is at the peak of the anacrotic limb. All of the illustrations show the dicrotic notch, in various positions on the dicrotic limb. One notes, however, that its position in time in the pulse wave is rather constant: from point .32 to .36 second from the beginning of the upstroke of the dicrotic notch. This time factor is rather important in the interpretation of this notch, as will be pointed out in the text.

estimates of the arterial blood pressure in infants under the age of one. In infants the systolic blood pressure is estimated from the pressure necessary to obliterate the pulse, and the diastolic blood pressure is estimated at the pressure at which maximum excursions occur. Figure 3 illustrates observations on a 1 year old infant during a Potts-Smith operation.

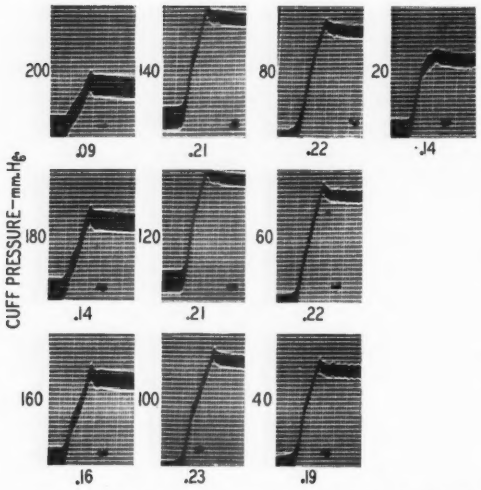


Fig. 5. Calibration recordings were made by placing the rubber cuff of a standard blood pressure instrument around a 3 inch tube. The cuff had previously been filled with 200 cubic centimeters of water and all air excluded. One outlet of the cuff had been plugged and the second outlet was connected to a 2 cubic centimeter syringe. The pickup mechanism of the oscillometer was then wrapped over this rubber cuff and recordings taken at cuff pressures as indicated in the record in the usual manner when 2 cubic centimeters of water was injected into the rubber bag. In this way a type of calibration is obtained which may not be as accurate as one would desire but it does show that there is a rather linear type of calibration in the range of cuff pressures of normal blood pressure. It also shows the small amount of overshooting when the force is applied for the periods indicated.

SENSITIVITY STUDIES

The sensitivity of this instrument has been the subject of considerable interest to those who have observed it in use. This characteristic will be discussed in the following order: (1) resistance of the droplet of ethyl alcohol to motion; (2) measurements of lag; (3) effects of the speed of paper; (4) measurements of the natural period of the instrument; (5) response to rapid heart rates; (6) attempts at calibration including the degree of oscillometric changes and the degree of overshooting.

Measurements of the resistance of the droplet of ethyl alcohol to motion were made by placing the instrument on its side in such a way that the calibrated recording tube was vertical. The speed of the droplet of ethyl alcohol falling through the tube and the speed of a droplet of alcohol falling in air were recorded under the force of gravity of 750 millimeters of mercury at 22 degrees centigrade. The interval necessary for fall in the tube and that required for fall of an equal distance in air were virtually the same which observation is illustrated in Figure 4a. This evidence is an indication of the extreme sensitivity of the apparatus. Also of interest is the fact that high speed photography of the moving droplet indicated that the meniscus on each side of the droplet extends to the ends of the pipette and maintains its form through its entire movement. It is thought that the droplet changes form, not position, and that resistance to this change is against itself and not against the walls of the recording tube.

Attempts were made to measure the lag of the instrument by several different methods, but the best results were obtained by taking synchronous electrocardiograms with the arterial pulse wave of a patient with and without incorporating 50 feet of tubing into the system. By using the peak of the *R* wave of the electrocardiogram as a point of reference it was possible to measure the speed of the transmitting wave motion which is about the speed of sound. Thus the lag period of the instrument used was about 0.004 second.

The speed at which the photographic paper is run has an effect on the appearance of the record, as shown in Figure 4b. For rapid heart rates, the faster speeds made it possible to study individual pulse waves with greater ease and accuracy. The instrument has 8 speeds which can be rapidly interchanged and it also contains filters to control the light to compensate for the changing of speeds. Figure 4b is an illustration of a record obtained from 1 subject by using 3 different speeds. Note the difference in the appearance of the records.

Natural period. In any discussion of the interpretation of the arterial pulse wave, the natural period of the vascular system and of the recording device occupies a prominent part. The natural period of the vascular system of the arm has been computed to be between 3.6 and 4.86 (1). Various instruments of both high and low frequency have been used to measure the arterial pulse wave. Some believe that a very high frequency in-

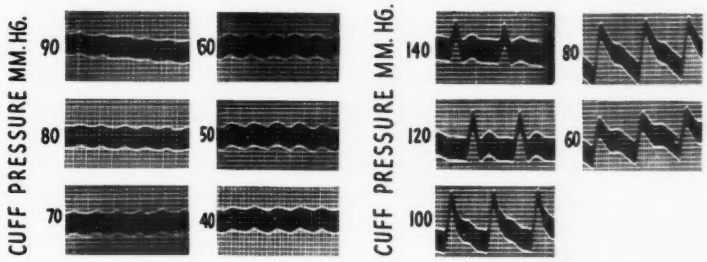


Fig. 6. Illustration of normal records. a, Taken from an infant at birth from the right leg, using an infant's blood pressure cuff. This was a breech delivery. The records indicate part of a study made during the delivery period of the fetus and were taken just after birth, but a large number were taken preceding this study. There is almost obliteration of the pulse wave at a cuff pressure of 90 and the maximum excursion occurs with a cuff pressure between 50 and 60, indicating that at birth the blood pressure is close to 90 systolic and between 50 and 60 diastolic. No other interpretations of this curve are given as this represents a study on a single case. It does, however, indicate that it is possible to obtain good records from the fetus as well as the infant at birth. b, Records taken from a white male, aged 17 years, with a blood pressure of 114/78. The records were taken above the right elbow. One notes that a very definite pulse wave is obtained well above the systolic pressure; also that as the pulse wave approaches the diastolic pressure, the amplitude is a maximum. Further, the character of the diastolic slope changes as one approaches the diastolic pressure to a line which might be compared to the hypotenuse of a triangle. In a large number of measurements, the correlation between this change in the diastolic slope and the auscultatory diastolic pressure was very consistent. In this patient the first notch is apparently buried in the anacrotic limb, but the dicrotic notch is well seen throughout the record. The crest time is measured from the beginning of the upstroke of the anacrotic limb to the peak of the first wave and this time has been most uniform when it is measured in records obtained with cuff pressures at or close to the diastolic pressure. Under these circumstances, the normal crest time has been close to .10 to .12 second in normal patients reclining and at rest. Records taken at the wrist, above the knee, below the knee, and at the ankle show these changes but usually to a lesser degree, with one exception—below the knee the amplitudes are usually greater than just above the knee or at the ankle. The explanation for this phenomenon is that the vascular bed spreads out through bifurcation of the popliteal artery such that the vascular bed is larger and can expand more freely than above the knee.

strument is absolutely essential for the accurate recording of the arterial pulse wave (11, 12) in order to minimize artefacts produced by the natural period and resonance in the recording instrument. For these reasons, we have done a great many experiments concerned with the natural period of the instrument under discussion which is a low frequency recorder.

The first experiments were concerned with measuring the natural period of the oscillometer while an artificial arm consisting of a 3 inch glass tube was used, but these results were unsatisfactory because they did not duplicate those obtained when similar experiments were done using the human arm. In the rigid system, mentioned, the natural period of the system was found to be 3.1[1] with cuff pressures ranging between 180 and 40 millimeters of mercury. It is of interest to note that the oscillometer is almost critically damped and an induced oscillation goes through only 1½ cycles before the recording droplet of ethyl alcohol comes to rest. Furthermore, the amplitude of the first part of the second cycle is only about 10 per cent of the primary oscillation.

These experiments were repeated in a nonrigid system using the human arm while records of the arterial pulse wave were made at various cuff pressures and during various phases of the pulse wave. When this was done, the induced oscillations went through only a single cycle before the recording droplet came to rest. Aside from the impressed volume change to produce the oscillation, the natural period of the instrument produced no

[1]The natural period of component parts may be much higher.

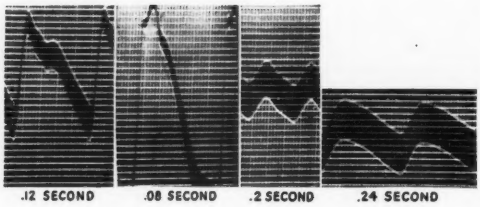


Fig. 7. These records, a, b, c, d, were taken at the diastolic pressure in 4 different patients to illustrate the crest time. a, b, and c, Taken above the elbow while, d, was taken above the knee. All records were taken with the patient at rest in the reclining position. The normal crest time is .12 second, a, while in the patient with aortic regurgitation, b, who also had congestive heart failure, the crest time was .08 second. The explanation for this difference is that in the second case the peripheral resistance had decreased out of proportion to the contraction of the left ventricle and hence a weaker heart can pump more blood against a decreased peripheral resistance than a strong heart against a strong peripheral resistance. c, The record from the patient with calcific aortic stenosis merely illustrates the slow emptying of the left ventricle in the presence of an obstruction to the outlet. Postmortem examination in this case indicated that the opening in the leaflets of the aortic valve was not much more than the size of the head of a match. d, The record of patient with occlusive arterial disease showed the slow crest time in the presence of occlusive arterial disease when records are taken distal to the occlusion. This is a very common finding in either partial occlusion or in the presence of extensive collateral circulation. This composite record illustrates the extreme importance of timing the events of the pulse wave in order that an accurate crest time can be measured. It seems as important to time the events of the pulse wave as it is to time the events of the electrocardiogram. The importance of this timing will be illustrated further in the analysis and interpretation of the pulse wave. In auricular fibrillation with congestive heart failure, the pulse waves may show irregular crest times; i.e., some crest times may be as short as .04 while others as long as .12 second. Also, in the presence of congestive heart failure, the amplitudes may be very large, indicating a very low peripheral resistance.

visible changes in the pulse record. In other words, this oscillometer acts virtually as an aperiodic recorder when it is used with a nonrigid system such as the human arm. The physicist who has done considerable work with the instrument considers this to be a desirable feature in contrast to a high frequency recorder.

The force and volume changes of the arterial pulse wave are transmitted to the recording droplet of alcohol by wave motion and without significant lag. The resistance of the droplet of alcohol to change form is thought to be only of a molecular nature. Studies with a device which acts as a mechanical heart show that the oscillometer accurately records induced changes. The sensitivity and low natural period of this device probably combine to reduce error to a minimum. At least, natural period and resonance do not interfere with the clinical usefulness of the oscillometer as will be shown later.

The sensitivity of this instrument to rapid heart rates is of interest. The most rapid ventricular rate which we have had the opportunity to record to date is 210, and in this record a secondary wave is recorded so that one can expect a sensitivity to rates of 420 per minute or more. A device used as a mechanical heart has a top speed of 250 beats per minute, and the oscillometer recorded this rate without fusion of beats or loss of sensitivity.

Attempts have been made to calibrate the instrument (Fig. 5) by using a 3 inch rigid tube and wrapping a standard rubber blood pressure bag partially filled with water around it. This is for the purpose of simulating the extremity, and records are made in the usual manner by the use of this system at various cuff pressures while 2 cubic centimeters of water are injected into the inner bag. The records show that within the range of normal blood pressure there is a reduction of volume change of about 10:1. Also, they show that the speed of the volume change influences the degree of overshooting. In a nonrigid system, because of the nature of the heart beat, the overshooting becomes a minor error.

In order to make further quantitative sensitivity studies, as well as to aid in the interpretation of normal and abnormal records, a precision device which acts as a mechanical heart has been constructed. No attempt will be made to describe this device in detail here because of space limitation, but it shows the following:

1. By means of a system of electrical and optical recordings the oscillometer has negligible lag.

2. Rates to 250 beats per minute show no fusion and no loss of sensitivity of the recording.

3. The normal human arterial pulse wave can be reproduced in every detail from mathematically computed cams. This shows that

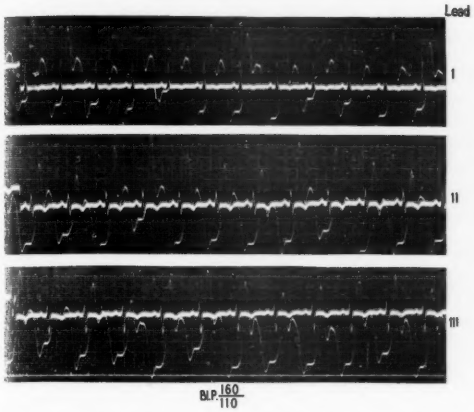


Fig. 8. Synchronous records of the electrocardiogram nd apex beat taken from a patient with hypertensive eart disease. There is a very close correlation between he *T* wave of the electrocardiogram and the dicrotic notch nd wave of the apex beat, indicating that the two phe- omena may be very closely related and both may be due o an active contraction of the heart at this time in the ardiac cycle. This explanation may offer a more reason- ble basis for the understanding and genesis of the *T* wave f the electrocardiogram.

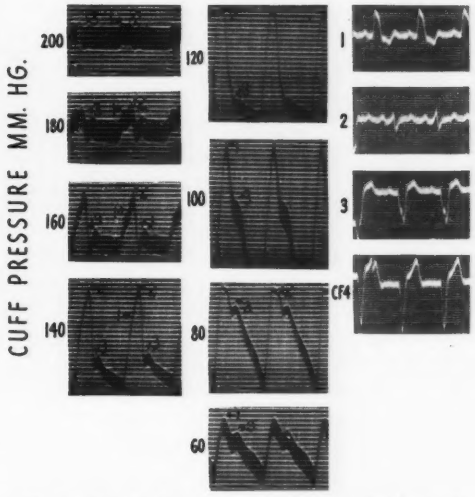


Fig. 9. Bundle branch block in patient 67 years old, blood pressure 172/98. This record is shown mainly to illustrate the genesis of the first and second peaks of the pulse wave. It was taken in the right arm above the elbow and shows that with increased cuff pressures the first notch appears on the anacrotic limb and as the cuff pressures are reduced there is a progression of the first peak to the apex where it remains. One notes in this record the second peak remaining at or close to the apex of the pulse beat throughout, also the position of the third wave or what is commonly known as the dicrotic wave. The position on the dicrotic limb varies somewhat with the cuff pressure used; however, in time it remains in the same position. This record is offered as evidence that the cause of the first peak is probably due to the first fraction of ventricular contraction while the second and third waves are caused by booster contractions

the oscillometer follows accurately the pulsatile arterial pressure changes without distortion.

4. Abnormal human arterial pulse waves can be reproduced in every detail by the mechanical heart.

5. The mechanical heart should be useful in the study of cardiovascular dynamics. It should be useful in determining the characteristics of other types of oscillometers used for recording pulsating phenomena.

THE NORMAL RECORD

The character of the normal record varies because of such factors as site of measurement, age, physical status, and environment. Studies have been made on numerous normal subjects in various age groups in which are included records from the newborn to the extreme age of 93. In order to aid in the interpretation of the normal record, many studies had to be made on patients with various types of cardiovascular disease, and, in addition, a device used as a mechanical heart had to be constructed in order properly to test the equipment and aid in the interpretation of normal and abnormal records. The records from normal patients and from those with abnormalities of the cardiovascular system show pulse waves which have several components common to both types of cases. These include amplitude, time of rise to the first peak called the crest time, the first notch, the second peak, the dicrotic notch, followed by the diastolic wave, and finally the diastolic slope. The interpretation of the arterial pulse wave is given in the following paragraphs in this order.

THE INTERPRETATION OF THE ARTERIAL PULSE WAVE

Amplitude. The amplitudes vary within a wide range with age, physical status, and locations from which the records are taken. Usually, the records decrease in amplitude

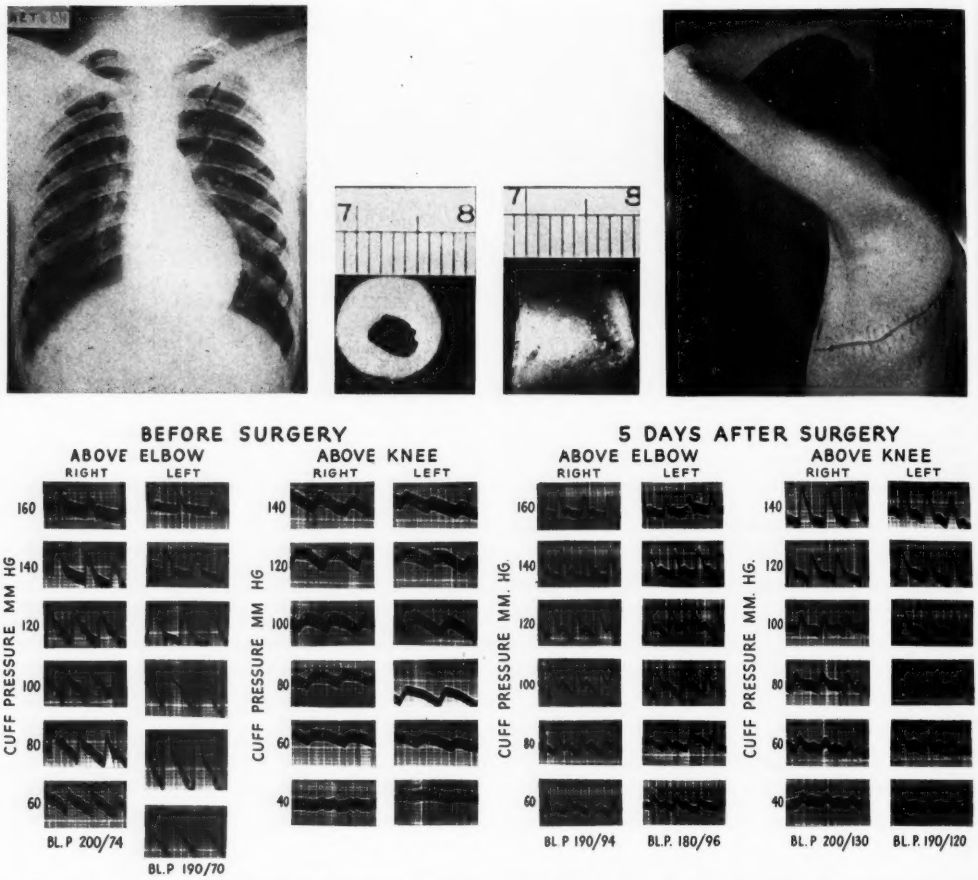
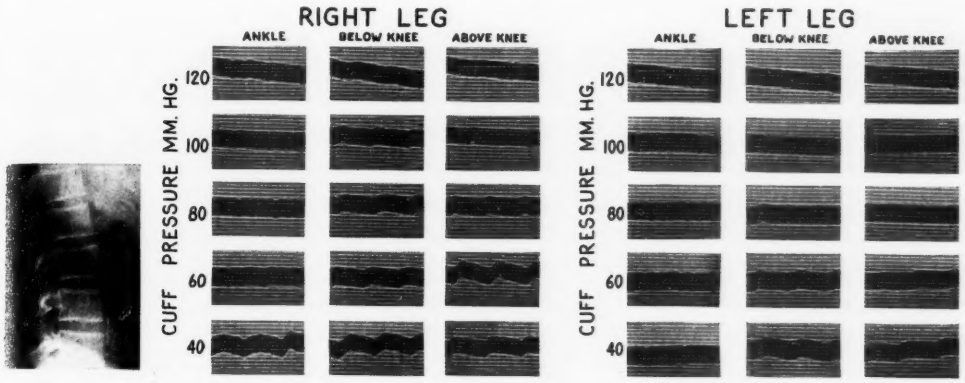
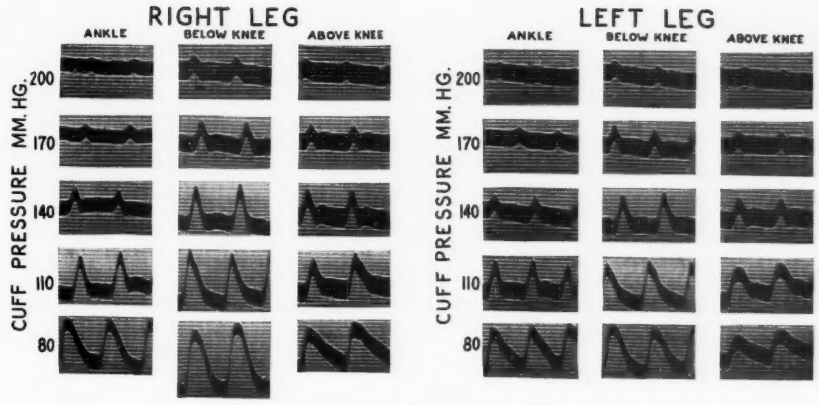


Fig. 10. A composite study taken from a 17 year old white male who had a proved coarctation of the aorta. Preoperative studies indicated the hypertension in both arms and an inability to obtain an auscultatory blood pressure in the legs. The records from the arms are what one would expect in hypertensive heart disease, but the amplitude in the left arm was somewhat greater than in the right due to anatomical differences observed at operation. The records from the legs indicated that the blood pressure was at least 140 millimeters of mercury or more despite the fact that the auscultatory blood pressure could not be obtained. This was partially verified at operation by palpating the distal aorta. One also notes from the records a long crest time in the legs of approximately .2 second as compared with a normal of .12. The amplitudes were less than normal, also. A resection of the aorta was done by Doctor John Reynolds in which the chest was open for 5 hours. The specimen is shown. Records were taken during the entire surgical procedure as well as at the regular intervals following the operation. The records taken 5 days after the surgery indicated that the records in the arms were approximately what one would expect in hypertensive heart disease while those in the legs had returned to a normal type of curve. Furthermore, the peripheral arteries in the legs could be palpated and the auscultatory blood pressure were obtained at 200/130 in the right leg and 190/120 in the left leg. Further experience with this method of study in coarctation of the aorta and the various anomalies of the cardiovascular system may indicate its usefulness in this type of cardiovascular disease.

the more distally they are taken from above the arm or above the knee. When taken with cuff pressures at the diastolic pressure there is one striking difference: records taken just below the knee are usually of higher amplitude than those just above the knee. In a 17 year old normal subject, the amplitudes observed with cuff pressures at the diastolic pressure



a



b

Fig. 11. a, These records were obtained from a patient with occlusion of abdominal aorta (Dr. Fremont Chandler's patient). The patient was a 50 year old white male with symptoms of severe intermittent claudication in both legs. None of the arteries in the legs could be palpated and an accidental deep cut in one foot produced virtually no bleeding. A lateral roentgenogram of the abdomen revealed marked calcification of the abdominal aorta as illustrated. Repeated recordings of the pulsatile arterial circulation gave only minimal pulsations as compared with normal patients. Also the crest time is markedly increased, indicating that the pulsatile arterial circulation in the legs is practically all of a collateral nature. However, x-ray evidence of marked calcification of the abdominal aorta is not good evidence of the degree of patency of the abdominal aorta as shown in other patients. A complete study as shown is important in determining the circulatory status before any contemplated surgery on the legs is done. b, These records of the pulsatile arterial circulation were obtained from the legs of a patient with occlusion of the abdominal vena cava (Dr. Roskelly's patient). The patient is a 46 year old white female who suffered from 9 known pulmonary emboli from a bilateral thrombophlebitis in her legs. Dr. deTakats ligated the abdominal vena cava 4 years ago following which the patient made a slow recovery. The patient has had very little edema for the past 2 years and has been able to work a full day. These records are shown to contrast them with those of a patient with deep femoral thrombosis shown in Figure 12 who had marked increased arterial pulsations in the affected leg. The explanation for the difference is not immediately apparent.

when converted to cubic centimeters were as follows: right arm above elbow 1.6 cubic centimeters, at the wrist 1.4 cubic centimeters, right leg above the knee 1.6 cubic centimeters, below the knee 3.8 cubic centimeters, at the ankle 1.6 cubic centimeters, at the instep 0.6 cubic centimeter. The amplitudes are greatest with cuff pressures at the diastolic pres-

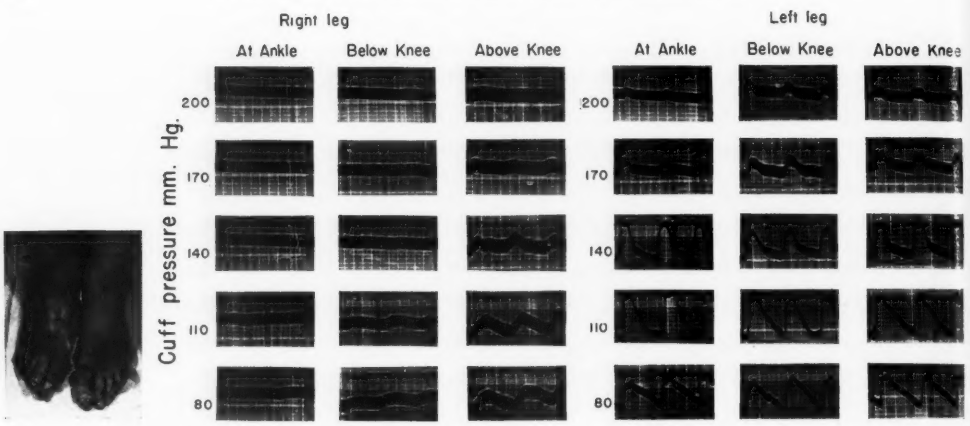


Fig. 12. a, Occlusion of the femoral artery. These records were made from the legs of a 66 year old white male who had a sudden occlusion of the right femoral artery associated with gangrene of the fifth toe. The oscillometer readings were made at the ankle, below the knee, and above the knee in both legs. One notes the normal type of arterial pulse waves in the left leg while in the right leg at the ankle there were virtually no oscillations; below the knee there were only slight oscillations with a long crest time and above the knee the oscillations were reduced in amplitude and with the crest time of .24 second, indicating that even at this site most of the arterial circulation was of a collateral nature. The femoral artery on the right side was palpable. On the basis of these findings, it was predicted that the occlusion was about mid-thigh. An amputation was done at this site and the occlusion was found to be at the site of the operation. The record is shown for two reasons: the first, in order to illustrate the type of record which the patient obtains in the presence of collateral circulation, and, the second, to illustrate the manner in which these records can be of assistance in the localization of arterial lesions.

sures, and this finding is in keeping with those of others (11). The striking changes in amplitude associated with diseases of the cardiovascular system will be discussed under individual diseases.

Crest time. The crest time is measured from the beginning of the anacrotic limb to the first peak which may be prominent or buried in the anacrotic limb on its ascent, or it may be at the peak of the anacrotic limb. In normal individuals reclining and at rest the crest time is approximately .12 second. In patients with congestive heart failure or vasodilatation the crest time may be as low as .04 second. In aortic stenosis the crest time may be as long as .24 second. In occlusive arterial disease with collateral circulation, the crest time taken distal to the occlusion may be as long as .24 second. These findings are illustrated in Figure 7.

There seems to be some correlation between the crest time and the amplitude of the excursions. If the peripheral resistance is lowered compensatory to cardiovascular disease, as in congestive heart failure, acute coronary occlusion, or following extreme vasodilatation, the crest time may be markedly decreased and the amplitudes increased. This phenomenon is illustrated in Figure 7 from a patient with congestive heart failure and in Figure 15 from a patient in whom an extreme vasodilatation was produced by the ingestion of 1½ ounces of whiskey.

From these studies it seems that the crest time is a very important component of the arterial pulse wave. One notes that it is an important measure of the peripheral resistance in relation to the action of the heart. Also it is important in estimating the degree of arterial occlusion as well as the degree of collateral circulation established.

First peak. The position of the first peak varies somewhat with the cuff pressure used and also varies considerably with the type of cardiovascular disease under study. In normal patients and in patients with cardiovascular diseases, it may be prominent or may be buried in the anacrotic limb. In normal patients and in most patients with cardiovascular disease it is usually found at the

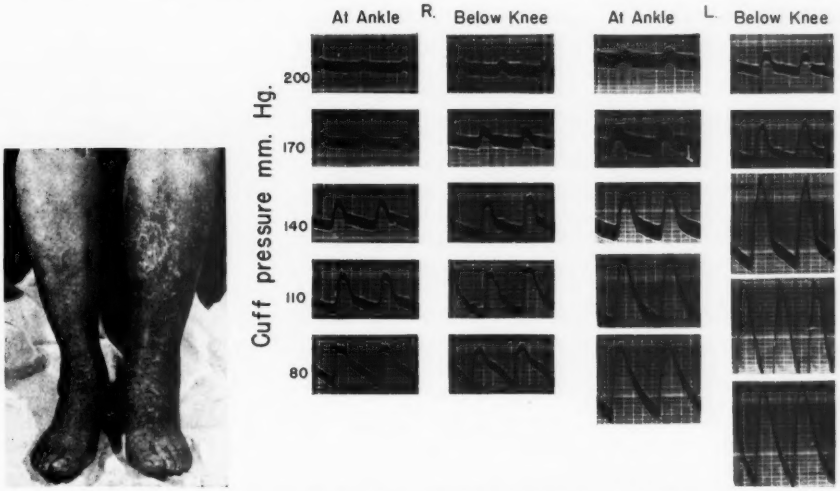


Fig. 12. b, Occlusion of the femoral vein. These records are from the legs of a colored female 63 years of age who had had a deep femoral vein occlusion 20 years before. The oscillometer readings were taken at the ankle and below the knee. One notes that in the left leg the marked swelling of the leg, discoloration, and the arterial pulse wave amplitudes are markedly increased. The explanation of this is not immediately apparent but it does indicate that occlusions of the veins may influence the type of record one obtains. This fact must be considered in the interpretation of the pulsatile arterial pulse wave.

height of the excursion of the arterial pulse wave. In 2 patients with bundle branch block, 2 patients with complete heart block, and 2 patients with aortic regurgitation and congestive heart failure, the evolution of the first peak could be observed upon the anacrotic limb depending upon the cuff pressure used in making the records. However, this was not a universal finding in these types of cases. Recordings of this progression of the first peak in the anacrotic limb are illustrated in Figure 9.

The cause of this peak has been the subject of a great deal of controversy. Some think that it is due to overshooting; some that it is related to the natural period of the vascular system; some that it is due to the natural period of the recording system; while others to a combination of the natural period of the recording system and vascular system; others think that it is due to some rebound phenomenon; and still others that it can be due to the results of the primary contraction of the left ventricle and that it represents the first component of the left ventricular contraction. It is possible that this first peak may be influenced by overshooting when the peak is at the height of the contraction, but it is difficult to see how overshooting can influence this peak when it is located half way up the anacrotic limb, as shown in Figure 9. A discussion and review of the literature can be found in Wiggers' (11) book on *The Pressure Pulses of the Cardio Vascular System* and he himself thinks it is due to a sudden change in the velocity of the blood. The present data would lead the author of this article to believe that it is related to the first fraction of ventricular contraction.

It is important to have an accurate understanding as to the cause of the first peak because it may lead to a better understanding of the nature of ventricular systole. It may be possible that in certain cardiac diseases one can have a relative failure of the first component of cardiac contraction without failure of the other components.

Third peak or dicrotic wave. This notch is usually located on the dicrotic limb. It usually occupies about middle position on the dicrotic limb but may be higher or lower and even in extreme vasodilatation may appear to

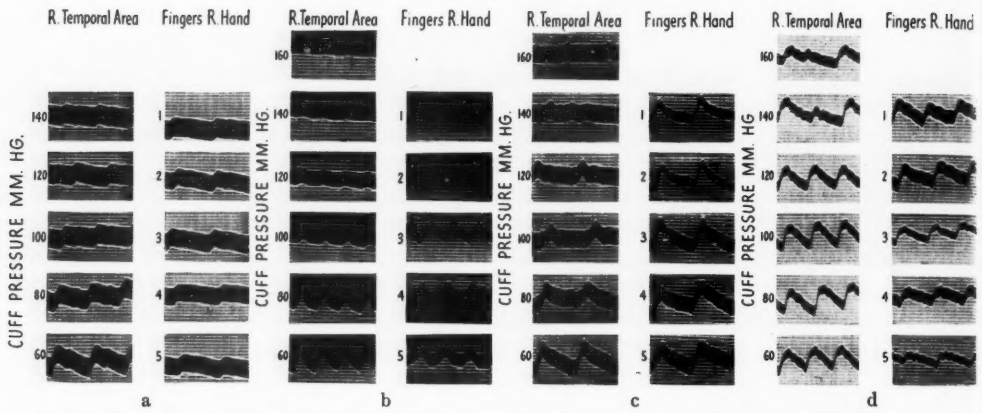


Fig. 13. These records are shown merely to illustrate that in the fingers as well as the temporal area the pulse wave can be recorded, and the character of the pulse wave with regard to amplitude is comparable to what is obtained elsewhere; however, it is partly different in its contour. No systematic study has been made with this instrument of the pulse wave of the temporal area. However, some preliminary studies in migraine indicated that there was a difference in the amplitudes on the affected side. a, Records taken in a normal patient; b, in a patient with aortic stenosis; c, in a patient with aortic regurgitation: d, in a patient with benign hypertension.

be on the anacrotic limb of the next beat. In time, it occurs about .32 second after the beginning of the pulse wave. It is related in time to the *T* wave of the electrocardiogram. It is also related in time to the dicrotic notch and wave as measured on the apex beat. Figure 8 illustrates synchronous records of the electrocardiogram and the apex beat and shows a very close relationship between the *T* wave of the electrocardiogram, the dicrotic notch and wave as measured on the apex beat, and also, by inference, the dicrotic notch and wave on the pulse wave.

The cause of the dicrotic notch and dicrotic wave is also subject to a great deal of controversy. Some think that it is due to the natural period of the vascular system or the recording mechanism; others, to a rebound phenomenon from the periphery; while others, to a rebound phenomenon associated with the closure of the aortic valve; still others, to an active contraction of the heart. According to the work of Sprague the aortic valve closes after the onset of the *T* wave and also after the onset of the dicrotic notch, and it does not seem that this closure of the valve could be the cause of the dicrotic notch. From the experimental data at hand it would seem that both the *T* wave of the electrocardiogram and the dicrotic wave of the pulse wave are a result of active contraction of the heart. Wiggers (11, 12) gives a general discussion of the literature on the subject. He thinks it is due to two factors: (1) transmission of a dampened incisura, and (2) superposition of the trough of a summated reflected wave.

The importance of these studies is that they would offer a more rational explanation for the genesis of the *T* wave (7) and also give further information on mechanical systole of the heart. From this discussion, it would seem that the heart has a primary contraction followed by two boosters, the first associated with the first peak and the second associated with the dicrotic wave. It is obvious that further work will have to be done to substantiate these ideas.

Diastolic slope. The diastolic slope is modified by the cuff pressure used. With cuff pressures above the diastolic pressure, the slope is more precipitous. With cuff pressures at or below the diastolic pressure, the slope is continued over to the next beat similar to the hypotenuse of a triangle. The pressure at which this occurs can be measured rather accurately and thus a method of accurately recording the diastolic pressure is given. As mentioned before, the maximum amplitude

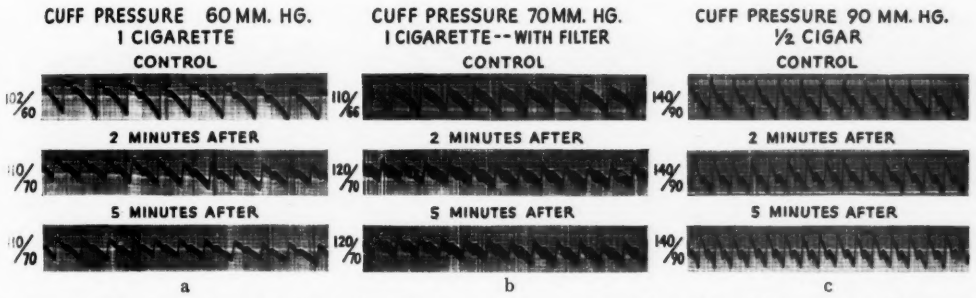


Fig. 14. The type of response obtained when records are taken from above the right elbow in patients who are sensitive to tobacco. A control record is taken following which the patient smokes a particular brand of tobacco that is under test. After discontinuing the smoking, a second record is taken and the blood pressure recorded. Likewise, a similar record is taken 5 minutes after. One notes that there is a decrease in the amplitudes of the excursions and this can occur with or without blood pressure changes and with or without changes in heart rate. A close analysis of the record indicates, however, that there is some increase in the crest time usually from a normal of .12 to .16, indicating an increase in the peripheral resistance. Records on patients who are not sensitive may show no change whatsoever in the oscillations. a, b, Case 1, patient, aged 32 years, with irritable bowel. c, Case 2, patient, aged 51 years.

of the pulse wave occurs at the diastolic pressure and at that position in which the diastolic slope continues evenly to the beat. This is in keeping with the principles set forth by Marey.

Some of the principles presented in the previous discussion can be used to good advantage in the interpretation of abnormal records. Although extensive studies have been made on all types of cases, only those bearing on surgery will be presented. Two, illustrating the effects of vasoconstriction and vasodilatation, will be shown.

ABNORMAL RECORDS

Coarctation of the aorta. The patient on whom these studies were made was a 17 year old boy in whom the diagnosis of coarctation was discovered accidentally. The boy was examined preliminary to entering competitive sports. The school doctor discovered a hypertension, and further studies indicated a diagnosis of coarctation of the aorta. Numerous studies were made preoperatively, during the surgery, and postoperatively. The operation was done by Doctor John Reynolds and took approximately 7 hours, during 5 hours of which the chest was open. A composite illustration of preoperative and postoperative studies in both arms and both legs, and illustrations of the chest, showing the scalloping of the ribs, and of the resected aorta are shown in Figure 10. Briefly, the records show hypertensive types of curves from the arms as well as greater amplitudes from the left arm which were due to an anatomical difference in the arterial blood supply in the two arms discovered at operation. Preoperatively, no auscultatory blood pressures could be obtained from the legs, and none of the peripheral arteries could be palpated in the legs, although the pulsatile arterial records indicated the blood pressure to be above 140 millimeters of mercury. This abnormal picture was partially confirmed during surgery by palpating the distal aorta. The records from the legs showed low amplitudes and long crest times, indicating a collateral type of circulation. The studies were repeated 5 days postoperatively and the pulsatile arterial records had returned to normal amplitude and crest time, the peripheral arteries could be palpated, and the auscultatory blood pressures could be obtained. In other words, the pulsatile arterial record had changed from that seen in a patient with extensive collateral circulation to that of a normal patient. By a method to be described later, the speed of the pulse wave from the heart to the knee was measured in this case and found to be .24 second while the normal averages approximately .17 second. Three other patients who had coarctation of the aorta also showed this prolonged rate of the pulse wave from the heart to the knee. With the accumulation of data and with further

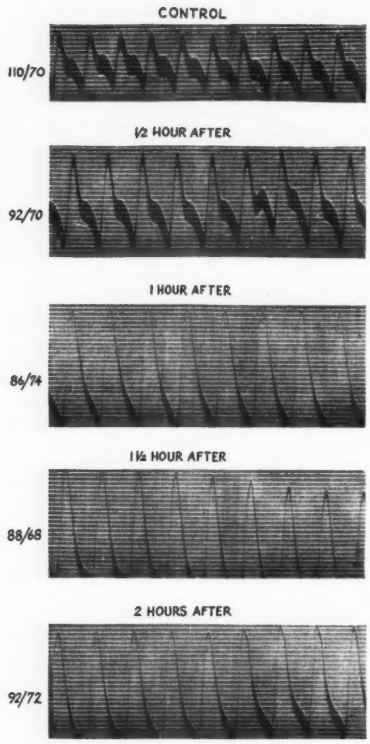


Fig. 15. These records were made from above the right elbow (with cuff pressure of 70 mm. Hg) in a white male, aged 42, who is sensitive to alcohol. The patient gave a history of having swelling of his mucous membranes following the ingestion of alcohol. A control record was made following which the patient drank 1½ ounces of scotch with water. Serial records were then taken at half hour intervals for 2 hours. Note the markedly increased amplitudes following the ingestion of scotch as well as the markedly decreased crest times from the normal of .12 to .08. Also note that there was some fall in blood pressure. The results of these studies in this patient indicate that, at least in this patient, alcohol produces a marked increased vasodilatation with a decrease in the peripheral resistance. Studies on other patients have not revealed as marked a response as in this patient, but in virtually all cases there is either no change at all or a moderate increase in the amplitude of the excursions following ingestion of alcohol. No systematic study has been made of the various brands of alcohol, or ethyl alcohol itself.

measurements of coarctated areas in comparison to the speed of the pulse wave from the heart to the knee, it may be possible to compute the approximate size of the coarctated area preoperatively. It is obvious that this idea will have to be confirmed by further studies.

Occlusion of the abdominal aorta. In 1 patient studied whose abdominal aorta was easily visualized by x-ray examination extensive calcification was demonstrated. Furthermore, neither the femoral arteries, popliteal arteries, dorsalis pedis arteries, nor posterior tibial arteries could be palpated, and the patient complained of rather severe intermittent claudication. Figure 11a shows the pulse records from this patient which indicate a very low amplitude, long crest time, and a totally inadequate type of pulsatile arterial circulation. However, the nonpulsatile arterial circulation apparently was able to sustain life of the tissues with a limited amount of physical activity. One must point out, however, that x-ray evidence of extensive calcification of the abdominal aorta is really no indication of its functional capacity since in other patients with extensive calcification of the abdominal aorta, records indicate almost a normal type of pulsatile arterial circulation in the legs.

Occlusion of the femoral artery. Records from a 66 year old, white, male patient with sudden occlusion of the right femoral artery are shown in Figure 12. Gangrene of the fifth toe developed. The femoral, popliteal, dorsalis pedis, and posterior tibial arteries could be palpated on the left side, but only the femoral artery could be palpated on the right side. Records of the pulsatile arterial circulation were taken above the knee, below the knee, and at the ankle in both legs. One notes a normal type of pulsatile arterial circulation of the left leg. In the right there were virtually no pulsations at the ankle, below the knee there were only small oscillations with a long crest time of .24 second, and above the knee the amplitudes were low with the long crest time of .24 second, indicating that the arterial circulation above and below the knee was of a collateral nature. On the basis of these findings, it was predicted that the arterial occlusion was about mid-thigh. An amputation was done at this site by Dr. Fremont Chandler, and the occlusion was found to be at the site of the amputation. In this patient the amputation was done at the site of the occlusion, but in another patient surgery was done

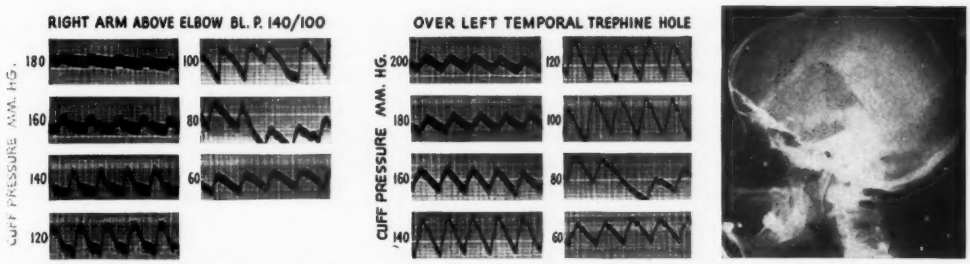


Fig. 16. Records of the pulsatile arterial circulation were obtained from a patient who had had a brain tumor removed about 1 year before the records were taken. Note in the skull picture the large trephine hole. The series of records on the left were obtained from the right arm above the elbow. The blood pressure was 140/100. The series of records taken over the left temporal area over the trephine hole indicates that it took more than 200 millimeters of mercury to neutralize the pulsatile arterial changes from the brain. An entirely different character to the pulse wave indicates possibly that the brain has some cushioning effect upon the pulsatile arterial changes. It is difficult to interpret these records in view of the above changes, because it does bring out the idea that a person may have a cerebral hypertension in the absence of a hypertension in the extremities. Similar records can be obtained during the actual surgery from the brain itself since the pickup mechanism can be sterilized and the records taken in the operating room. It is obvious that no conclusion can be drawn from a single case and further study may bring out facts which may make it possible more accurately to interpret these records.

below the site of occlusion, a patent artery was found, and injection of a radio-opaque material into the arterial bed revealed by x-ray examination a patent arterial system. Further vascular study of the amputated stump again suggested the occlusion to be above the site of amputation. In 6 patients studied by this method, this last case was the only one in which a possible error occurred.

Occlusion of the femoral vein. This record is included to illustrate some of the difficulties in interpretation of arterial records. Figure 12b illustrates records from a patient with occlusion of the left deep femoral vein with edema and discoloration of the leg. One notes the tremendously increased amplitudes on the affected side. No explanation for the changes observed are offered at this time as it is obvious that further studies will have to be made.

OTHER STUDIES

Records from the temporal artery. Figure 13 shows a composite study of records taken from the temporal artery in a normal patient, in one with aortic stenosis, in one with aortic regurgitation, and in a patient with hypertensive heart disease. These records have a different appearance than those taken in the extremities, but no systematic study has been made of this difference. The usefulness of this type of record has not been determined, but in 1 case of unilateral migraine the amplitudes on the affected side were less than those on the unaffected side.

Effects of smoking. The effects of smoking have been studied in a number of patients, but no systematic study has been made in a large group of controls. Figure 14 shows a composite study on 2 patients who were sensitive to tobacco. It is our observation that if a patient is sensitive to one form of tobacco smoke, they will show the same sensitivity to smoke from tobacco processed in different ways, whether it is denicotinized or altered in other ways. Also, there seems to be no tolerance developed as far as this reaction is concerned. The observations have been made that the amplitude changes may take place with or without heart rate changes, or with or without measurable blood pressure changes. Close examination of the records has revealed that the crest time becomes increased as the amplitude decreases in contrast to the effects of alcohol reported in the following.

Effects of alcohol. A number of studies have been made following the ingestion of alcoholic beverages, but no systematic study of the effects of alcohol itself has been made. Figure 15 illustrates one such study in a patient who was sensitive to 1½ ounces of Scotch whisky given in water. One notes from the record the tremendous increase in amplitude and de-

crease in crest time, indicating a marked decrease in the peripheral resistance which would be interpreted as a vasodilatation. In general, most patients over the course of 2 hours following the ingestion of 1½ half ounces of whiskey show no change or a slight increase in the amplitude. The patient from whom the record was made showed other allergic manifestations to the ingestion of the type of liquor for which he was tested. The response may be more in the nature of a sensitivity or allergy to this particular type of liquor. In other words, this response should not be interpreted as the typical response to alcohol, but possibly an allergic response in this particular patient. The record is shown mainly to illustrate the relationship between the crest time and the amplitude.

The cerebral arterial circulation. In the presence of a trephine hole of the skull, records of the cerebral arterial circulation can be made. Figure 16 illustrates 1 such case from a patient in whom a tumor of the brain had been removed about 1 year before the records were taken. One notes from Figure 16 a control record is illustrated from the right arm above the elbow with cuff pressures from 140 to 60 and a second record taken over the trephine hole, indicating possibly that the brain has a cushioning effect on the arterial pulsations. In addition, it took over 200 millimeters of mercury to neutralize the arterial pulsations over the trephine hole, which fact indicates the possibility that a person may have a cerebral hypertension in the absence of a hypertension in the extremities. This explanation is probably inadequate from observations upon a single patient, and it is obvious that it may be incorrect, and also as obvious that a great deal more work will have to be done in order to determine the usefulness of this method of studying the cerebral arterial pulsatile circulation.

Observing the surgical status of the patient. It has been pointed out that the pulsatile arterial changes can be projected on the screen in patients from birth to old age. With a little practice one can note the pressure at which obliteration of the pulse takes place, the pressure at which the oscillations are the greatest, and also the presence or absence of arrhythmias. This procedure is particularly useful in infants when surgery is absolutely essential. In infants, if the point of obliteration of the pulse wave is considered to be at or close to the systolic pressure and the point of maximum excursion the diastolic pressure, a curve can be drawn of the pressure changes throughout surgery. In the patient from whom the record illustrated in Figure 3b was taken, arrhythmias always preceded fall in both systolic and diastolic pressures. In this particular patient, surgery was absolutely essential. There did not seem to be any other comparable procedure by which it was possible continually to estimate the surgical status of the patient. This procedure may be useful for the purposes which are outlined for this particular patient.

Study of the circulation of the fetus during delivery. The various changes which take place in the fetal circulation during delivery can be studied in breech deliveries. At the moment the leg is born, a sterile infant's cuff can be placed upon the leg and connected to the instrument, and records can be taken at whatever intervals seem desirable in order to obtain a better understanding of the changes which take place during this process.

Records of the pulsatile arterial circulation made with the patient at a remote distance from the instrument. By incorporating a long piece of tubing, that is to say as long as 50 feet, into the system, it is possible to make recordings of the pulsatile arterial circulation without much loss of sensitivity with the patient 50 feet from the instrument. This may be of some use when the instrument is being used as a lie detector and when it is essential that the patient not observe the procedure as it is being carried out. Or it may be useful in various procedures in the operating room when it is not desirable to have the instrument close to the patient.

Records of the pulsatile arterial circulation taken from a submerged extremity. The pickup mechanism of the oscillometer is waterproof and watertight, and it is possible to take records from an extremity submerged in water. No systematic study has been made but this should offer a simple method of study of many problems in physiotherapy, as well as

a method of study on the physiological effects of submersion of the body in hot or cold water.

DISCUSSION

It is difficult to discuss this paper since no single phase of the subject is complete except possibly the development of the instrument itself. In this regard one may say that this simple portable device, which requires virtually no training to operate, opens up many new problems in cardiovascular physiology and has many clinical applications. The studies thus far have been mainly of an exploratory nature.

However, a few comments may be in order in regard to what this instrument measures. It measures volume changes as well as the time of these volume changes which are a reflection of the pulsatile arterial flow of blood as compared to the nonpulsatile flow. The meaning of the various components of the arterial pulse wave have been briefly discussed and further work is in progress to determine, if possible, the genesis of these components. The factors which influence the pulse wave have been studied and one may tentatively say that they are the result of cardiac and vascular activity, mainly the strength of the heart beat in relation to the peripheral resistance. In normal people under usual conditions a definite balance is maintained which allows for the emptying of the left ventricle within a time which has been fairly constant in the subjects studied. In severe myocardial disease, the body may compensate by decreasing the load on the heart as a result of decreasing the peripheral resistance, such that a weak heart may actually pump the same or a greater volume of blood per beat in less time than the normal. These findings probably account for the conflicting reports on the cardiac output in congestive heart failure reported in the literature reviewed by Harrison. In the presence of collateral circulation, the crest time is prolonged above the normal to as much as .24 second.

A brief statement as to the usefulness of this instrument may be indicated. Records taken with this instrument give information regarding the mechanical activity of the heart, just as the electrocardiogram gives information regarding the electrical activity of the heart. Each record is useful in its place, and it is just as important to time the components of the mechanical wave as it is to time the components of the electrical wave. From numerous observations in this study, one can say that in most instances the electrical and mechanical records do not parallel each other in the information given concerning cardiovascular activity.

Considering the instrument from a surgical point of view, it should be useful as a diagnostic aid in distinguishing functional from organic arterial occlusion, localizing arterial occlusions, determining the degree of collateral circulation, estimating preoperatively the severity of coarctation of the aorta, observing continuously the surgical status of the infant patient, and in observing the progress of treatment. It should lend itself very well to certain experimental studies on various conditions, such as surgical shock, the relative toxicity of various anesthetic agents, and the cerebral circulation. In obstetrics, the instrument is useful for studies on the mother and fetus during birth as well as on the mother and infant after birth.

SUMMARY AND CONCLUSIONS

The results from studies of the pulsatile arterial circulation with a new, simple, accurate, portable instrument have been presented. No single phase of the subject has been completed except the perfected instrument. The results of an exploratory study of the usefulness of the oscillometer in experimental pharmacology and physiology, as well as in experimental and clinical surgery, have been presented.

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ANOMALIES OF THE FIRST BRANCHIAL CLEFT

LOUIS T. BYARS, M.D., F.A.C.S., and ROBIN ANDERSON, M.D., St. Louis, Missouri

CONGENITAL anomalies of the branchial apparatus have constituted an interesting problem since Rathke provided the first accurate description of the embryology of the region in 1825. Particularly during the last 40 years (3, 5, 7, 8, 10), the surgical literature has contained numerous reports on the derivation, diagnosis, and treatment of these abnormalities. It is interesting to note, however, that while the common type of branchial anomaly—derived from the second or third branchial cleft, and known variously as branchial, branchiogenic, or lateral cervical cyst, sinus or fistula—has been well investigated, comparable defects of the first branchial cleft have been mentioned only rarely. In reviewing 82 cases of branchiogenic anomalies, Ladd and Gross found only 1 which they considered of first cleft derivation. Hyndman mentions without explanatory discussion an unusual case reported by von Berg in which a sinus tract, whose external opening was at the thyroid notch, presumably communicated with the middle ear. In the Mayo Clinic series of 319 cases (9), no first cleft anomaly was encountered. In view of the apparent rarity of this abnormality, it would seem worth while to present the following report of 3 cases.

From the Department of Surgery, Division of Plastic Surgery, Washington University School of Medicine, St. Louis, Missouri.

EMBRYOLOGY (1)

During the fourth embryonic week, five ridges known as branchial arches, separated by grooves called branchial clefts, appear on the ventrolateral surfaces of the head of the human embryo (Fig. 1a). Comparable entodermal pouches develop from the rudimentary pharynx, bulging laterally to meet the ectodermal grooves between the arches. Thin plates, consisting of a layer of mesoderm between the ectoderm of the groove and the pharyngeal entoderm, are thus formed. It is presumed that these plates remain intact.

Each branchial arch develops a cartilaginous core, a blood vessel (aortic arch), and various muscles and nerves. The vessels of the first two arches soon disappear, while those of the third and fourth arches persist as the internal carotid arteries, the right subclavian artery, and the aorta. The first branchial arch bifurcates into maxillary and mandibular processes. From the maxillary process ultimately develop the lateral portion of the upper lip, cheek, maxilla, part of the palate, parotid gland, and

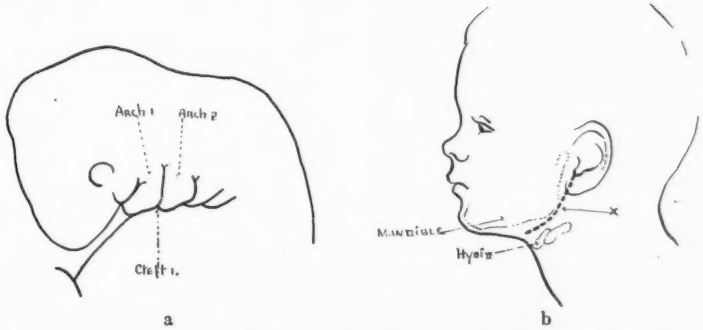
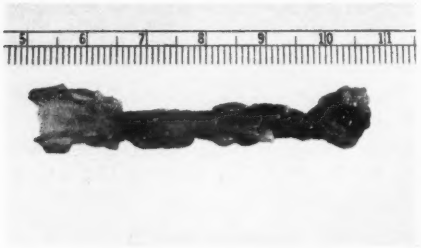


Fig. 1. a, Schematic drawing of 5 week human embryo (after Arey) showing initial development of the branchial arches and clefts. b, Schematic drawing showing structures derived from the first and second branchial arches. The approximate site of the embryonic first cleft is shown as a heavy broken line (*x*), and marks the expected position of an anomaly derived from this cleft.



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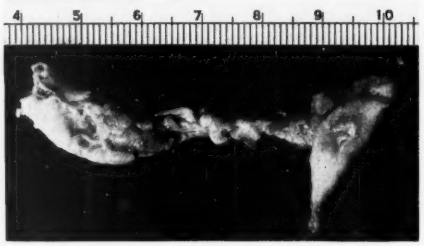

b

Fig. 2. a and b, Photographs of surgical specimens which were obtained in first and third cases described, showing prominent cuff of cartilage at point of previous attachment to ear canal.

the ventral or anterior half of the auricle. The mandibular portion gives rise to the lower lip, soft tissue of the lower jaw, the mandible, submaxillary and sublingual glands, portions of the tongue and palate, and the malleus and incus. The second arch provides the dorsal half of the auricle, soft tissue of the upper neck, the stapes and styloid process, and the lesser horn of the hyoid (Fig. 1b). During the sixth embryonic week, the second arch grows, overlapping the more caudal arches and grooves. The ectodermal cavity, or cervical sinus, thus produced normally disappears. The consensus of modern opinion ascribes the usual branchial cleft cyst or fistula to the persistence of this cavity, with an opening into the pharynx via the remnants of the second cleft (2, 6).

From the first branchial pouch develop the lining of the middle ear, the mastoid cells, and the eustachian tube. Its corresponding ectodermal groove produces the external auditory canal and the outer surface of the tympanic membrane. An anomaly of the first cleft thus should be found high in the neck, above the level of the hyoid, below the lower border of the mandible, and probably opening into or in close proximity to the external auditory canal.

CLINICAL DATA

Three examples of this anomaly have been encountered. The first was in a 16 year old white female with a history of having had a cyst below the angle of the jaw opened surgically at the age of 6 months. The cyst had continued to drain, along with a persistent ear discharge, until time of entry. The second patient was a 1 year old infant who was first seen shortly after the unsatisfactory incision and drainage of what had been interpreted as a jaw abscess. The third patient, a 19 month old girl, presented a history of occasional drainage from a small opening below the middle third of the left mandible. This drainage was usually accompanied by a purulent discharge from the left ear canal.

In the 2 cases in which the neck lesion was associated with an ear discharge, the diagnosis of first cleft anomaly was made prior to operation. In the third case, the diagnosis became evident only at the operating table.

TREATMENT AND DISCUSSION

Surgical excision of the lesion with the patient under general anesthesia is the treatment of choice. The injection with mild pressure into the external orifice of a half and half mixture of methylene blue and hydrogen peroxide may be useful in outlining the course of the tract during the dissection. An elliptical incision around the external opening, in the plane of the skin crease, is made and the tract gradually dissected free. It is followed posteriorly beyond the angle of the mandible, and then upward through the parotid gland. Care is taken to avoid injury to the cervical branch of the facial nerve in this area. When further dissection through the anterior incision becomes difficult, a second incision is made along the anterior border of the ear, extending slightly onto the neck (Figs. 3 and 4). The anterior surface of the tragal cartilage is followed inward. It is essential that the face be watched carefully throughout this part of the procedure

to note any twitches caused by direct stimulation of the facial nerve. Any questionable tissue is tested by gentle pinching with forceps before it is cut. When the termination of the tract in the ear canal is encountered, dissection is continued anteriorly and downward through the substance of the parotid until the previous plane of dissection is reached and the tract is free except for its attachment to the ear canal. The cuff of cartilage extending from the ear canal onto the sinus tract is excised with the specimen (Fig. 2). No attempt is made to close the cartilaginous defect in the ear canal.

From the embryologic standpoint, it is difficult to predict the relationship of the main stalk of the facial nerve to a first branchial cleft anomaly. Because the nerve leaves the brain via the second arch, and terminates in the area derived from the first arch, it is obvious that at least part of it must cross the anomalous tract directly in front of the ear or within the substance of the parotid. However, one can only guess as to whether this crossing will be medial or lateral to the tract. In the 1 case in which the facial nerve was exposed by dissection during the operation, the trunk of the nerve was immediately lateral to the tract, looped over the cartilaginous cuff in a more superficial position than normal (Fig. 3). All branches of the nerve distal to the main trunk were anterior to the tract. Specific exploration of the nerve was not felt to be warranted in the other 2 cases.

Microscopic examination of the 3 surgical specimens showed stratified squamous epithelium with hair follicles, sebaceous and sweat glands, lining the tract. This is in agreement with the common findings on examination of other branchial cleft anomalies and would further establish the ectodermal origin of the lesion.

The question arises as to why so few of these first cleft anomalies have been observed and described in the literature. One might surmise that in the hands of inexperienced surgeons, tracts which extend so far as apparently to disappear in the substance of the parotid gland might be lost or excised before their termination in the ear. It is difficult to imagine this course of events happening to a skilled operator. In all probability, a significant number

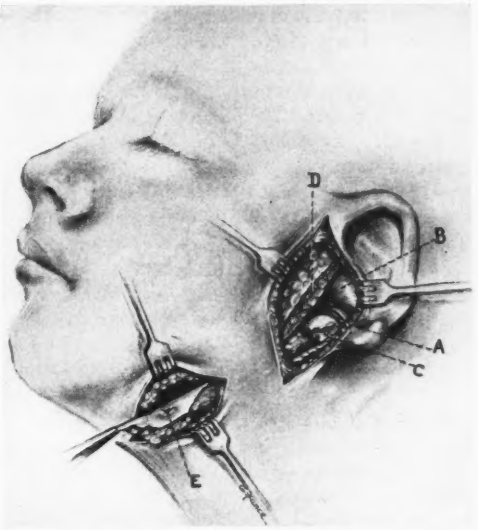

Fig. 3. Drawing of operative field showing the two incisions necessary for dissection of the sinus tract. The facial nerve is seen looping over the cartilaginous cuff. *A*, Facial nerve; *B*, tragal cartilage; *C*, cartilaginous cuff (termination of tract); *D*, cut edge of parotid gland; *E*, external orifice of tract.

Fig. 4. Photograph showing location of incisions and their closure.

of these defects has been successfully treated, and filed away under "Miscellaneous."

The foremost factor in making the diagnosis of a first cleft anomaly would be keeping in mind the possibility of such a lesion in the patient with a cystic swelling or draining fistula high in the neck. An accompanying ear discharge without middle ear infection and a ruptured eardrum would be confirmatory. Furthermore, one should often find the opening of the sinus into the ear canal if a specific search were made of the anterior, inferior wall of the canal, particularly at the point of juncture of its outer third with the inner two-thirds.

SUMMARY

The embryology of the branchial apparatus has been reviewed, with special reference to the formation of anomalies of the first branchial cleft.

Three examples of this anomaly have been described. The criteria of diagnosis and the surgical treatment have been outlined.

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ADENOMAMMECTOMY FOR BENIGN BREAST LESIONS

CARL O. RICE, M.D., F.A.C.S., and J. H. STRICKLER, M.D., Minneapolis, Minnesota

BLOODGOOD has stated that simple mastectomy is a procedure which is too radical for benign lesions and inadequate for carcinoma.

Radiating incisions or incisions which are made directly over a suspected tumor are inadequate from many points of view. Such an incision is unsightly; it does not allow for adequate examination of the surrounding breast tissue; bleeding is excessive because of the inadequacy of exposure through the small, deep dissection. If, in doing a biopsy, carcinoma has been encountered, the infiltrating portion of a carcinomatous tissue may be cut through and thus provide the possibility of implantation of carcinoma cells. Many benign breast tumors may be multiple (cystic mastitis) and the incisions mentioned make it impossible to explore or remove more than the one tumor that had been palpated.

The Warren incision or the Gaillard Thomas incision has been described for the removal of benign tumors. Perhaps the cosmetic value of this type of an incision has been overemphasized to the detriment of its more valuable features, as it appears that this incision is too infrequently used for biopsy or the removal of benign tumors in preference to a less adequate radiating incision.

The Warren incision (Fig. 1), which can be made in the mammary-thoracic fold on the under surface of the breast, can be advantageously extended to one side or the other, depending upon the extent of the breast exposure that is desired. All or any portion of the mammary gland can be examined or removed through this incision.

The dissection can be extended upward upon the pectoral fascia to the uppermost portion of the breast tissue. By everting the breast over the fingers (Fig. 2), the entire posterior surface of the mammary gland can be examined. With the surface of the breast exposed in this manner, radiating incisions can be made into the breast substance from the posterior surface in any area if it is desired to explore the breast substance.

When an isolated tumor is palpated, the entire tumor and surrounding breast substance can be excised and the remainder of the mammary gland can be more adequately explored by palpation and inspection than through the skin from without. If multiple cystic disease of the breast is found, all of the breast tissue can be removed without deviating the approach and without simple mastectomy; thus when the nipple and contour may be preserved the surgeon need not be reluctant to remove all of the mammary gland so that a patient with cystic disease need not face a future of recurrent bumps and repeated biopsy excisions.

If carcinoma is found, this incision lends itself to radical mastectomy by using a similar upper ellipse and a vertical extension into the shoulder as illustrated in the inset (Fig. 1).

TECHNIQUE

The incision is made in the mammary thoracic fold and is extended from one side to the other as becomes indicated. The incision extends down through the skin and subcutaneous fat to the pectoral fascia (Fig. 1). The breast is then dissected off from the pectoral fascia and the dissection is carried upward until the isolated tumor is passed (Fig. 2), or when complete adenomammectomy is desired the dissection should continue upward until the entire mammary tissue is dissected from the pectoral fascia (Fig. 3). By blunt separation, such as by spreading a scissors, small vessels are avoided and the main blood supply to the breast may be isolated and clamped.

After the tumor has been passed, an incision is made into the mammary substance at its uppermost margin to cut toward the subcutaneous fat (Fig. 3). The dissection is then directed back toward the skin incision while an attempt is made to cut parallel to the skin

Fig. 1. A Warren incision in the mammary-thoracic fold on the under surface of the breast is made down to the pectoral fascia. The inset demonstrates conversion to radical mammectomy.

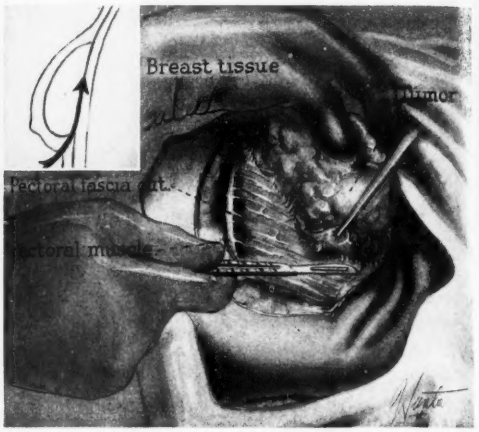

Fig. 2. The dissection is carried upward along the surface of the pectoral muscle as the left hand of the surgeon evaginates the breast tissue and rolls the redundancy into the palm of his hand.

surface and keep the dissection within the "breast capsule" until the tumor has been excised with a portion of the surrounding normal breast tissue (Fig. 4).

As the surgeon holds the breast flap in his left hand (see illustrations) the guiding finger can evaginate the breast and at the same time identify the tumor as it is being excised.

It is important that 1 or 2 millimeters of "breast capsule" be left with the subcutaneous tissue. If this is not done and if the excision extends into the subcutaneous fat, subsequent

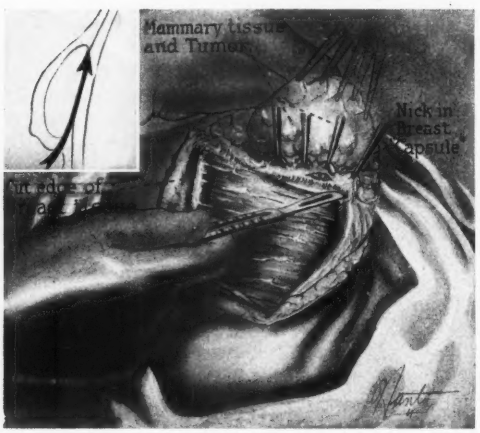

Fig. 3. At the upper edge of the mammary gland or beyond the isolated tumor the breast tissue is grasped with a row of forceps in order to pull the breast tissue away from the subcutaneous tissue. The breast tissue is then cut with sharp dissection from the anterior fibrous breast "capsule." As this step progresses an occasional nick can be made into the "capsule" to determine that no glandular tissue is being left behind.

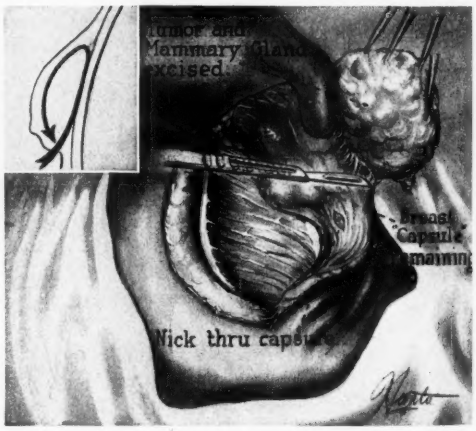

Fig. 4. The adenomammectomy being nearly complete, the skin, subcutaneous fat, and breast "capsule" have been preserved and will be replaced to maintain a normal contour. Nicks through the breast capsule indicate the nearness of the subcutaneous fat. Leaving the breast "capsule" is important lest scar tissue adhesions cause puckering of the skin to the chest wall. When the capsule is left intact this does not occur.

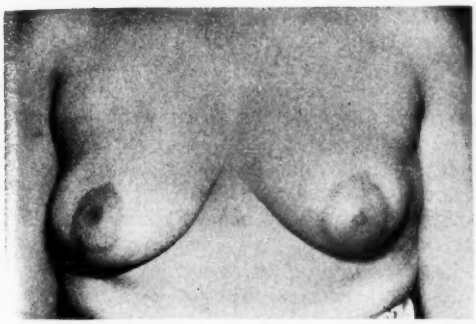

Fig. 5. Subtotal adenomammectomy as a mammoplasty or unilateral hypertrophy. Preoperatively right breast was about twice as large as left. Here—8 weeks after operation.

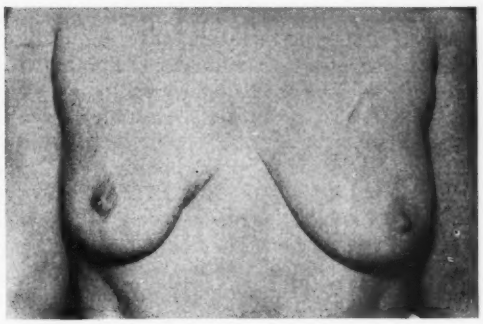

Fig. 6. Right adenomammectomy for adenocystic disease. Six months after operation. All the glandular tissue has been removed.

healing will leave puckering deformities with cicatricial adherence of the skin to the chest wall. The plane of this dissection can be identified by the smooth, whitish, glistening membranes lying directly beneath the subcutaneous fat. A small nick through this fibrous tissue membrane into the yellow subcutaneous fat can occasionally be made to identify the depth of the dissection (Fig. 3). The inset in each drawing illustrates the progression of the mammary gland enucleation.

Bleeding is controlled with the endothermic coagulator so as to obtain a very dry field. This condition, too, is important lest subsequent oozing result in a slowly developing hematoma. Meticulous hemostasis by this means is essential. The surgeon should not be satisfied short of a completely dry field.

When complete adenomammectomy is desired because of the multiplicity of benign lesions, as in adenocystic disease, then the entire breast substance is dissected from beneath the "breast capsule" (Fig. 4).

In cases of hypertrophy the affected breast can be proportionately reduced in size in this simple manner. Excellent cosmetic results have been obtained by partial or complete adenomammectomy through this type of incision. Such a plastic incision is well hidden beneath the mammary thoracic fold (Fig. 5).

If a suspected cancer is being biopsied the entire primary lesion and surrounding breast tissue should be excised, and the malignant lesion should be cut into only after it has been removed. In this manner, the disadvantages of cutting through carcinomatous cells are obviated.

If the lesion is found to be malignant, an upper ellipse with a curved vertical extension into the shoulder region readily transforms this operation into a radical mastectomy procedure (inset of Fig. 1).

If the lesion is benign the breast flap is replaced onto the chest wall and the skin edges are approximated with clips or everting sutures. A drain is brought out through the lateral end of the incision.

No deep sutures are used to reapproximate the edges of the mammary gland from which a local lesion has been excised, nor is any attempt made to fill in the defect which is left by the excision of a local lesion. The cut upper edge of breast tissue should be beveled off lest a shelf-like deformity remain when the breast is replaced onto the chest wall. The palpating hand over the replaced breast flap will identify any such edges. No subcutaneous stitches are used as they, too, would add to the induration and disfigurement of suture line.

A smooth, flat, brassiere type of dressing is applied over the replaced breast holding it in its normal rounded contour. When these details are meticulously adherred to, the breast contour returns to normal though it is somewhat smaller (Fig. 6).

This procedure (adenomammectomy, partial or complete) has been performed in 64 patients for benign disease in the past 5 years. In all instances the breast contour has been satisfactorily retained.

COMMENT

In performing an operation for tumor of the breast, the surgeon should always be prepared initially to do the operation of election. This should be the case whether the tumor proves to be benign or malignant. The patient should be advised of the possibility of doing a radical mastectomy for malignancy and the operative preparation should be made accordingly. If facilities are not available for making a complete diagnosis at the time of the initial operation, the patient should then be referred to a hospital where such facilities are available rather than be subjected to two separate operations.

With the type of approach which has been described herein, the entire posterior surface of the breast can be examined. When multiple cystic disease is found a complete adenomammectomy can be done. It seems unjustifiable to do a simple mastectomy for benign lesions which do not have their origin in skin or subcutaneous tissue since they can be excised by adenomammectomy as adequately and without disfigurement.

CONCLUSIONS

Complete adenomammectomy can be accomplished through an extended Warren incision.

In doing a complete adenomammectomy, if the "breast capsule" is left with the subcutaneous fat, the replaced flap will assume an essentially normal contour and no disfigurement will thereby result.

A more adequate exposure and a more satisfactory biopsy can be obtained from the under surface of the breast through a Warren incision than is possible through a radiating incision over the breast surface.

A Warren incision can be converted to a radical mastectomy by making an upper ellipse and vertical extension into the shoulder. A transverse ellipse for excision of the breast in radical mastectomy with a vertical arm extending into the shoulder allows more skin for covering the defects of a radical mastectomy than can be accomplished through a vertical ellipse.

If it is desired to examine the entire breast substance, this can be accomplished through a Warren incision, whereas the radiating incision over the breast allows exploration of only small portions of the breast tissue.

When multiple cysts are encountered, an adenomammectomy is the operation of choice since excision of a single mass will frequently be followed by additional masses necessitating subsequent biopsies; simple mastectomies are a great deal more disfiguring.

Adenomammectomy simplifies mammoplasty for breast hypertrophy and accomplishes proportionate diminution of size in case of simple hypertrophy.

THE SEX HORMONES IN FRACTURE HEALING

An Experimental Study

W. RALPH DEATON, JR., M.D., FRANK FORSYTH, M.D., T. O. COPPEDGE, M.D., and H. H. BRADSHAW, M.D., F.A.C.S., Winston-Salem, North Carolina

THE endocrinological literature contains many articles concerned with the effect of the estrogens and androgens on bone formation and density in animals, and a few articles on the clinical use of these sex hormones to promote fracture healing. There are no significant comparative studies, either clinical or experimental, to demonstrate the effect of the sex hormones, in addition to the usual supportive measures, in the treatment of fractures. The following experiment was designed to produce such a comparative experimental study.

METHOD

Eighteen mongrel dogs were used, with the sexes divided evenly. Preoperative determinations of the weight and serum protein, calcium, phosphorus, and alkaline phosphatase were made. With the dog anesthetized (intravenous pentobarbital) and under sterile precautions, the midpoint of the left radius was exposed, without cutting any muscles, and was divided with a Gigli saw. The wound was closed with interrupted catgut sutures. A sterile dressing and adequate padding were placed on the leg, followed by tongue blade splints and heavy adhesive tape. The dogs were allowed to ambulate at will. At 2 week intervals the weight and blood chemistries were determined, and roentgenograms, both anterior-posterior and lateral views, were taken of the fracture site. Seven weeks postoperatively, the involved leg was amputated and the radius dissected out. The breaking strength of the bone at the fracture site was determined with the apparatus shown in Figure 1.

The dogs were divided into 3 groups, with each group consisting of 3 males and 3 females. The dogs in group I did not receive any medication; those in group II received 25 milligrams of testosterone propionate (perandren) twice weekly, while those in group III received 1 milligram of estrogenic substance (alpha-estradiol dipropionate—ovocylin) twice weekly. All medications were given intramuscularly with sterile technique. The amounts used are comparable, on a weight basis, to the suggested human therapeutic dosage. No antibiotics were used; no infections occurred. Diet consisted of the usual kennel ration, a commercially prepared complete dog food in biscuit form.

From the National Cancer Institute and the departments of Surgery, Orthopedics, and Radiology, Bowman Gray School of Medicine of Wake Forest College.

RESULTS

The results of the blood chemistry studies, weight changes, and x-ray interpretation of callus formation are shown in Charts 1 through 5 and Table I. Figure 2 shows the guide used for interpreting roentgenographic changes. The breaking strengths of the isolated bones are shown in Table II.

INTERPRETATIONS

The absence of significant changes in the tested chemical constituents of the blood was not unexpected. Levin and Smith demonstrated that the blood calcium levels in mam-

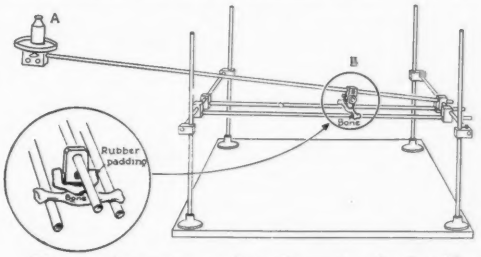

Fig. 1. Apparatus used to Determine the breaking strength of the healing fractured bones. Weight is added at *A* in 100 gram increments until the bone breaks. The amount of force applied is then determined by replacing the bone with a balance and actually measuring the force.

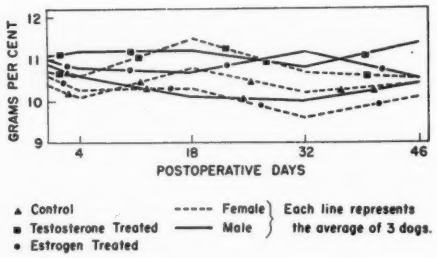

Chart 1. Serum calcium levels.

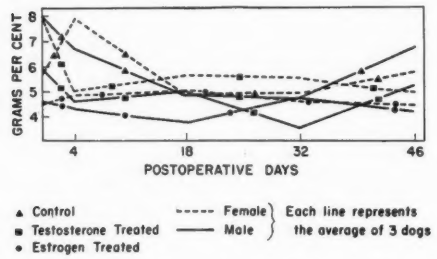

Chart 2. Serum phosphorus levels.

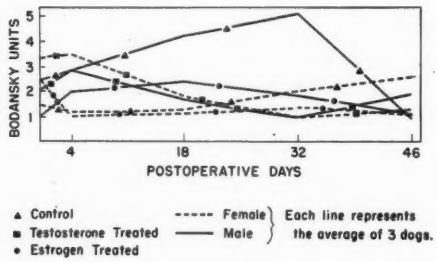

Chart 3. Serum alkaline phosphatase levels.

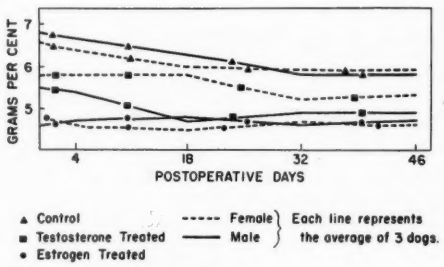

Chart 4. Serum protein levels.

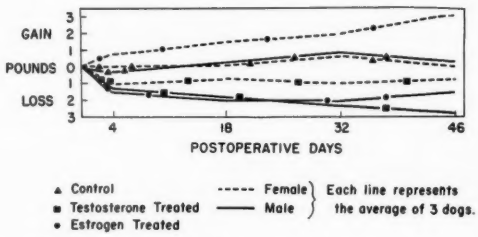

Chart 5. Weight variation.

mals, in contradistinction to what has been shown in egg laying animals (3), are unaffected by estrogenic administration. It is reasonable to assume that androgenic administration would likewise have no effect on the calcium level. With calcium and phosphorus being interdependent, disruption of the phosphorus level would hardly be expected with a normal calcium level. The sudden large shifts in the alkaline phosphatase levels in the male control group are surprising and not explainable, unless due to laboratory technique error, for in each case the high average was due to an extremely high level in one of the dogs (a different dog each time). The serum protein levels remained constant, within the realm of laboratory error. The weight variation was no more than has been found in this laboratory in dogs that were essentially normal, and being kept for long term experiments. The average amount of callus formation shows an almost constant value for all 6 groups. Although the difference in the means of the breaking strength of the male control group and the male testosterone treated group is large (3,493 gms.), it is not large enough to meet the test of mathematical significance (the difference between the means did not equal, as a minimum, at least twice the standard error of the difference between the 2 means). The difference in the means of other comparable groups is even less significant.

DISCUSSION

The majority of experimental work on the effect of the sex hormones on osteoblastic activity has been with egg-laying animals, which of necessity have a quite labile calcium regulating mechanism to allow for rapid de-

TABLE I.—AVERAGE CALLUS FORMATION, JUDGED BY ROENTGENOGRAPHY

Group	Sex	Postoperative days			
		2	16	30	44
Control	Male	0	1.3	2.0	3.0
	Female	0	1.0	2.0	2.3
Testosterone treated	Male	0	1.0	2.0	2.0
	Female	0	1.3	2.3	2.5
Estrogen treated	Male	0	1.3	2.3	2.5
	Female	0	1.0	2.3	3.0

Legend—0—Fresh fracture
1—Earliest discernible reaction
2—Minimal calcification
3—Callus
4—Strong union

TABLE II.—BREAKING STRENGTH OF HEALING FRACTURED RADII (IN GRAMS)

			Male	Female
Controls	Dog No.	1	9,710	3,710
		2	5,710	6,310
		3	14,000	4,900
	Mean		9,807	4,973
	Standard deviation		2,817	1,060
Testosterone treated	Dog No.	4	15,500	8,500
		5	11,100	4,000
		6	13,000	3,825
	Mean		13,200	5,442
	Standard deviation		1,750	2,305
Estrogen treated	Dog No.	7	10,607	6,500
		8	11,400	8,100
		9	9,800	3,700
	Mean		10,602	6,100
	Standard deviation		690	1,776

position of the egg shell (3). Consequently, this experimental work is not directly applicable to mammals. Further, the experiments to determine the change in breaking strength of bones of normal animals that have been treated with one or the other of the sex hormones have no bearing on the present experiment, which is concerned only with the effect of the hormones on fracture healing. Very little has been reported on this phase of the use of the hormones. Pollock, investigating the premise that ovarian function might influence calcification, did a short series of experiments on rats in which he apparently demonstrated a beneficial result of theelin administration on fracture healing. He used the humerus and did not apply any splints after the fracturing. His x-ray films show the involved bones to be in poor apposition and alignment, which undoubtedly influenced the results. A few years later Brush demonstrated that if the rat's fibula was used, with the tibia

Fig. 2. Scale used for interpretation of the roentgenographic changes: 0, fresh fracture; 1, earliest discernible reaction; 2, minimal calcification; 3, callus; 4, strong union.

acting as a splint, theelin actually delayed the occurrence of bony union. Hills and Weinberg had good results in the use of theelin clinically in 3 cases of nonunion and then sought laboratory confirmatory evidence, using both cats and dogs, relying upon the x-ray appearance entirely for interpretation of the rate of healing. They used the radius and depended on the ulna to splint the fracture. The results were not conclusive, nor as gratifying as the clinical results had appeared to be. Connolly published a review of the literature on the subject of estrogens as related to osteoblastic activity and reported his results in 9 cases. As he pointed out, in cases in which bone disease, such as osteoporosis, was present, theelin provided a great deal more stimulus to callus formation than when no bony abnormality existed. This observation is in agreement with the results which were obtained by Hills and Weinberg.

CONCLUSIONS

In normal, healthy, adult dogs, the use of the sex hormones has no demonstrable effect on experimental fracture healing, as determined by evaluation of (1) the roentgenographic changes, (2) pertinent blood chemistry findings, (3) weight fluctuations, and (4) breaking strengths of the tested bones.

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THE PROGNOSIS OF CANCER OF THE CERVIX BY VAGINAL SMEAR

Correlation with Five Year Results

RUTH M. GRAHAM, B.S., Boston, Massachusetts

IN an initial report (1) published in 1947 the effect of radiation on the vaginal cells in cervical carcinoma was described and the prognostic significance of these cellular changes was discussed. This report referred to a study of 73 patients with cervical carcinoma who were treated by irradiation. Vaginal smears were taken on these patients either during treatment or within 6 months after their treatment and studied for the amount of radiation change present.

Evidence of the radiation changes in the epithelial cells of the vaginal smears is as follows: vacuolization of the cytoplasm, increase in size of both nucleus and cytoplasm, appearance of two nuclei in a single cell, and nuclear changes such as wrinkling, irregularity of chromatin and of the nuclear border. These changes follow a time sequence, the vacuolization taking place first, reaching a peak 13 days after the beginning of radiation treatment, and then gradually disappearing. Size increase, double nuclei, and nuclear changes all reach a peak at about 24 days after beginning of x-ray treatment. The percentage of cells showing these changes is considered as an index of the degree of radiation effect present in the smear. In most cases during x-ray treatment the malignant cells disappear. We have found the presence or absence of malignant cells in the vaginal smear to be of little prognostic significance.

From a semiquantitative estimate of the number of epithelial cells showing radiation change, the cases were classified as good or poor radiation responses, prognostically. If the great majority of the *nonmalignant epithelial cells* in the vaginal smear showed radiation changes[1], the case was considered to be a good response. On the other hand, if only a few of the benign epithelial cells showed radiation effect, the case was considered to be a poor response.

At the time of publication of these 73 cases in 1947 the maximum time of follow-up was 3 years. It appeared important to re-examine this group of patients at 5 years. The present article is a report of the 5 year survival of the group.

In the original paper the prognostic accuracy in the entire group was 88 per cent if 3 patients with no follow-up were excluded. If the 3 patients with no follow-up were considered as errors, the accuracy was 83 per cent. As might be expected, the overall accuracy at 5 years is not as high as at 3 years, but the difference is not great, having changed only 8 per cent. We have been able to trace every one of the 73 patients and the absolute prognostic accuracy at 5 years is 75 per cent. (If 2 patients dying of intercurrent disease are excluded, the relative accuracy of prognosis is 80 per cent.) When the poor and good response groups are examined separately it becomes evident that the accuracy of prognosis differs widely in the two groups. Of 37 patients classified as poor responses, only 1 is alive. The prognostic accuracy in the poor response group is thus 97 per cent. Of 36 patients considered to be good responses, 20 are alive, or an absolute prognostic accuracy of 55 per cent, a relative accuracy of 60 per cent. It appears that if a patient with carcinoma of the cervix treated by irradiation does not show marked changes in the benign epithelial cells of the vaginal smear, her chances of surviving 5 years are slim indeed.

From the Vincent Memorial Laboratory of the Vincent Memorial Hospital (the Gynecological Service of the Massachusetts General Hospital).

[1]A detailed description of the cellular radiation change may be found in the initial report (1).

TABLE I.—STAGE I CASES
Good Response Group

Patient No.	Type and grade of tumor	Treatment		Living	Dead	Survival in months	Comment
		X-ray r*	Radium mgm. hr.				
G- 3. MR-429551	Epi. ca.	6000	4500	+		81	
G-13. MC-448361	Epi. III	6000	4400	+		80	
G-26. AL-429781	Epi. III	6000	4120	+		76	
G-29. LB-P10091	Epi. ca.	10000	5000		+	74	Metastatic disease found in cervical node
G-31. SH-P22013	Epi. ca.	4800	4355 +Wertheim	+		71	No tumor found at Wertheim

Absolute 5 year survival—80 per cent
Average survival in months—75
There were no poor responses in stage I
*Roentgens measured in air

Tables I, II, III, and IV give detailed information about the 73 cases. The number before each initial corresponds to the number of that patient in the original paper. The case numbers of the good responses are preceded by the letter "G"; the poor responses, by the letter "P." The cases have been divided according to stage of the disease by the International classification. It will be seen that there are no poor responses in stage I. This should not be interpreted as indicating that all stage I cases are necessarily good responses. In studying additional cases, poor responses have been found in stage I. Table V compares the 5 year survival of the poor and good response group according to stage of disease and is a condensation of the first 4 charts.

Table V shows that there is a great difference in survival between the poor and good response groups. For instance, in stage II, 65 per cent of the patients in the good response group are alive and without disease at 5 years, and all in the poor response group are dead. It should be pointed out that this is not a selected group of cases. They were selected only on the basis of whether a vaginal smear had been taken either during or within 6 months after radiation treatment. In 1950 Morris and Meigs reported on 377 cases of cancer of the cervix treated at this hospital from 1927 to 1942. The 5 year cure rate for the entire group was 24.7 per cent. The 5 year cure rate for these 73 patients was 30 per cent. The correlation between these two figures suggests that the smaller group of 73 included in this study is probably representative of carcinoma of the cervix treated in this hospital, since one might logically expect some increase in salvage rate over a 20 year period.

The obvious suggestion as to why these two groups of patients have reacted so differently is that they were treated differently, i.e., those in the good response group received adequate roentgen therapy; those in the poor response group did not. Admittedly, the uniformity in the treatment of these cases leaves something to be desired. Some patients received adequate amounts of radiation; others only palliative doses. Three patients had surgery in addition to their radiation, 2 a Taussig lymph node dissection and 1 a Wertheim type hysterectomy. Although adequate treatment is essential for a good outcome, lack of treatment cannot explain the poor response group. In Table VI the cases are divided according to the amount of treatment received. Six thousand roentgens of x-ray in air plus 3,500 milligram hours of radium is arbitrarily regarded as being adequate. Forty-six of the 73 patients received at least this amount of radiation. Of the 26 good responses receiving adequate therapy 58 per cent of the patients survived 5 years. Of the 20 poor responses receiving adequate therapy, only 1 patient, or 5 per cent, survived 5 years. Such a difference indicates that some other factor than the amount of radiation received was responsible for the great difference between the two groups.

Chart 1 shows the survival in months of both groups plotted according to the stage of their disease. Again, there is a significant

TABLE II.—STAGE II CASES

Good Response Group

Patient No.	Type and grade of tumor	Treatment		Living	Dead	Survival in months	Comment
		X-ray r*	Radium mgm. hr.				
G- 1. RC-439665	Epi. II	6000	3900	+		84	
G- 2. ER-439680	Epi. IV	6000	4500	+		71	
G- 4. RA-471575	Epi. III	6200	4000 +Taussig		+	47	No local recurrence. Tumor at bifurcation of aorta
G- 5. JG-483169	Epi. III	6200	4000		+	8	No evidence of local recurrence
G- 7. MJ	Adeno.	6000	4500		+	9	No evidence of disease. Probable radiation death
G- 9. AT	Adeno.	6000	3500	+		75	
G-10. LM-483419	Epi. II	7800		+		62	
G-12. LE-448883	Epi. III	6000	4440	+		69	
G-14. MR-439056	Adeno.	6000	4000		+	45	Metastatic disease in lumbar spine. No local recurrence
G-15. LP-469056	Epi. II	6300	2000	+		66	
G-16. LT-464874	Epi. III	6000	4500	+		64	
G-18. CA-P-21896	Epi. II	4800	3045	+		66	
G-19. AC-P-21988	Epi. II	6600	4500		+	20	Died of cardiorenal disease
G-21. AM-P-22017	Epi. II	6400[a]	3300	+		77	
G-24. MP-475340	Epi. III	6000	4000	+		68	
G-25. AS-441145	Epi. III	Exact amo unt not known.			+	21	Local recurrence
G-28. MR-442199	Epi. II	6000	4590	+		68	
G-32. DC-P-21866	Epi. II	6400[a]	2950 +Taussig	+		82	No + nodes at Taussig
G-34. LS-509225	Epi. II	6000	4000		+	10	No evidence of local recurrence
G-36. OW-465187	Epi. III	6000	4930	+		64	

*Roentgens measured in air
Absolute 5 year survival—65 per cent
Relative 5 year survival—72 per cent
Average survival in months—54
[a]The dose indicated in original paper was an error

Poor Response Group

P- 2. MD-359456	Undiff.	6000	1500		+	5	Local recurrence
P- 3. LS-438516	Epi. III	6000	3900		+	7	Local recurrence
P- 4. AW-422476	Epi. III	6000	3900		+	10	Local recurrence
P- 6. MH-446955	Epi. IV	6000	4100		+	36	Unknown whether local recurrence
P- 9. ME-443037	Epi. III	4000	4500		+	7	Local recurrence
P-13. MC-451643	Epi. III	6000	4500		+	19	Distant metastases
P-30. SB-P-22098	Adeno.	6400	4540		+	12	Unknown whether local recurrence
P-32. CY-P-21926	Adeno.	2800			+	27	Local recurrence
P-37. GP	Epi. III	6000	3200		+	31	Unknown whether local recurrence

Absolute 5 year survival—0
Average survival in months—17
Total number of cases—stage II—29
Absolute 5 year survival—40 per cent
Accuracy of prognosis—stage II—77 per cent

difference in the survival curves of the two groups. When the survival in months is plotted against the stage of disease, the good response group shows a straight decline. As would be expected, the stage I survives longest and there is a progressive decline in survival

TABLE III.—STAGE III CASES

Good Response Group

Patient No.	Type and grade of tumor	Treatment		Living	Dead	Survival in months	Comment
		X-ray r[b]	Radium mgm. hr.				
G- 6. MK-438206	Epi. ca. II	6000	4500	+		70	
G- 8. AR-439656	Epi. ca. III	7200	4000	+		71	
G-11. PV-449303	Epi. ca. III	4200	1680		+	19	Unknown whether local recurrence
G-20. MD-P-21936	Epi. ca. III	8400[a]	4500	+		68	
G-22. MS-P	Epi. ca.	7600[a]	4500		+	5	Unknown whether local recurrence
G-23. MC-409627*	Adeno.	6300	?		+	12	Unknown whether local recurrence
G-27. MS-439876†	Epi. ca. II	6000	4500		+	7	Distant metastases
G-33. MF-473195	Epi. ca. III	6000	4050		+	21	Distant metastases

*In original paper called a stage I. Actually a recurrence of a lesion which was originally a stage I. At time of smears, a stage III
†Reviewed: a stage III rather than a stage II
[b]Roentgens measured in air
Absolute 5 year survival—37 per cent
Average survival in months—35

Poor Response Group

P- 1. MK-486495	Epi. ca. IV	6000	4520		+	8	Local recurrence
P- 5. MB-456936	Epi. ca. II	4500	4400		+	10	Local recurrence
P- 8. BS-359869	Epi. ca. III	7200	4400		+	12	Local recurrence
P-10. KD-229221	Epi. ca.	2200			+	15	Local recurrence
P-11. MR-448198	Epi. ca. III	6000	3860		+	46	Distant metastases
P-12. EK-124387	Epi. ca. III	6000	4020		+	5	Local recurrence
P-14. LB-494748	Epi. ca. III	6000	4500		+	60	Distant metastases
P-17. AL-Pr. Pt. 10614	Adeno.	6000[a]	3700		+	21	Distant metastases
P-18. HD 425174	Epi. ca. III	6400			+	23	Distant metastases
P-19. RK-446757	Epi. ca. II	6200	3920		+	10	Unknown whether local recurrence
P-20. MF-435332	Adeno.	4000			+	11	Local recurrence
P-21. EF-458600	Epi. ca. IV	4100			+	3	Local recurrence
P-23. VC-Pr. Pt. 10607	Epi. ca. II	6000	4968		+	18	Unknown whether local recurrence
P-24. DA-Pr. Pt. 10896	Epi. ca.	5200	3115		+	4	Local recurrence
P-27. MM-452067	Epi. ca. III	6000	4500		+	78	Unknown whether local recurrence
P-28. DT-491046	Epi. ca. IV	6000	3960		+	3	Unknown whether local recurrence
P-29. BH-P-21625	Epi. ca. II	7600	3030		+	15	Unknown whether local recurrence
P-35. BT	Epi. ca. III	8200			+	5	Local recurrence
P-36. MH	Adeno.	6000			+	4	Local recurrence

[a]The dose indicated in original paper was an error
Absolute 5 year survival—0
Average survival in months—18
Total number of cases—stage III—27
Absolute 5 year survival—11 per cent
Accuracy of prognosis—stage III—82 per cent

time for each succeeding stage. The poor response groups do not show this gradual decline. The stage II patients died as rapidly as the stage IV. There is no significant difference between the average duration of survival of stage II, III, or IV patients. It is difficult to explain this uniformity.

It is of some interest to examine the persistence of local disease in these two groups of patients. In the good response groups there

TABLE IV.—STAGE IV CASES

Good Response Group

Patient No.	Type and grade of tumor	Treatment		Living	Dead	Survival in months	Comment
		X-ray r*	Radium mgm. hr.				
G-17. WM-503552	Epi. ca. III	2100	3750		+	10	Unknown whether local recurrence
G-30. WP-13115	Adeno.	7500			+	17	Extension of adenocarcinoma of rectosigmoid to the cervix
G-35. KL-172301	Epi. ca. II	6000	4000		+	30	Recurrence at introitus

Absolute 5 year survival—0
Average survival in months—19
*Roentgens measured in air

Poor Response Group

P-15. AM-499432	Epi. ca. II	6000	4500		+	12	Local recurrence
P-16. CT-346999	Epi. ca. III	6000	3700	+		65	
P-22. NT-494767	Adeno.	6000	4500		+	28	Local recurrence
P-25. ET-Pr. Pt. 10908	Epi. ca. III	?	4000		+	18	Local recurrence
P-26. DV-Pr. Pt. 11024	Epi. ca. II	?	?		+	12	Local recurrence
P-33. MP-P-21849	Undiff.	6400	4660		+	5	Local recurrence
P-34. MW-482066	Undiff.	6200			+	5	Local recurrence

Absolute 5 year survival—14 per cent
Average survival in months—21

Unknown Stage—Poor Response

P- 7. DS-483843	Epi.	6000	4620		+	1	Local recurrence
P-31. PG-P-22034	Epi. II	8400			+	9	Local recurrence

Total number of cases—stage IV—10
Absolute 5 year survival—10 per cent
Accuracy of prognosis—stage IV—60 per cent

were 16 deaths. Seven patients died of distant metastases, 2 of intercurrent disease, and 4 had local recurrence. In the remaining 3 it was impossible to tell from the record whether the patient had local recurrence or not. Two of the patients who had local recurrence were in stage IV. If we exclude the patients in whom it was impossible to say whether or not local disease was present, 4 out of 13 patients, or 30 per cent, had local recurrence. If we calculate these figures on the total group of good responses, 11 per cent of the group had local recurrence. In the poor response group 23 patients had local recurrence, 5 distant metastases, and in 8 it was impossible to say—thus 82 per cent of the patients with adequate data in the poor response group had local recurrence. These figures indicate that in the majority of good responses the local tumor is cured, while in the majority of poor responses, the local disease is not eradicated

ERRORS IN PROGNOSIS

Good response group. There were 16 deaths in this group of patients. Two patients died of intercurrent disease. Of the 4 patients dying with local disease present, 2 were not primary cases. One (Case G-30) was an extension of an adenocarcinoma of the rectosigmoid to the cervix. It is likely that the tumor was too far advanced to be destroyed by the radiation. The other (Case G-23) was a recurrence of a papillary adenocarcinoma of the cervix, treated originally by cautery. The significant radiation changes in the epithelial cells did not take place until the 30th day of treatment. We know now that this is much too late, and therefore this case should have been classified as a poor response. The prognosis in a third case (Case G-25) was made on 1 smear 4 months after treatment. This is asking too much of the method. Smears should be taken, preferably during the entire

TABLE V.—COMPARISON OF SURVIVALS IN GOOD AND POOR RESPONSE GROUPS

	Good	Poor	Entire group
Stage I			
No. cases	5	0	5
5 year survival, per cent	80		80
Stage II			
No. cases	20	9	29
5 year survival, per cent	65	0	45
Stage III			
No. cases	8	19	27
5 year survival, per cent	37	0	11
Stage IV			
No. cases	3	7	10
5 year survival, per cent	0	14	10
All stages			
No. cases	36	37*	73
5 year survival, per cent	55	3	30

*Plus 2 cases of unknown stage

TABLE VI.—COMPARISON OF SURVIVALS ACCORDING TO AMOUNT OF TREATMENT RECEIVED

	Good	Poor	Entire group
At least 6,000 r* and 3,500 mgm. hr. radium			
No. cases	26	20	46
5 year survival, per cent	58	5	35
Less than 6,000 r* and 3,500 mgm. hr. radium			
No. cases	7	8	15
5 year survival, per cent	57	0	27
No radium			
No. cases	2	8	10
5 year survival, per cent	50	0	10
Unknown			
No. cases	1	1	2
5 year survival	0	0	0

*Roentgens measured in air

course of treatment, or at least at the end of treatment, to be accurate from a prognostic point of view. The fourth case (Case G-35) of local recurrence was a stage IV. The tumor extended from the cervix to the vulva. After radiation the tumor in the cervix and vagina completely disappeared. Unfortunately, the tumor at the introitus was outside the field of radiation. It was here that tumor persisted and recurred. This patient was explored for an acute intestinal obstruction due to radiation fibrosis 18 months after her treatment and no evidence of tumor was seen in the peritoneal cavity. It would appear that this patient responded remarkably well to radiation but, because of the extensive nature of her original lesion, did not receive adequate therapy.

The 7 patients with distant metastases all had an adequate number of vaginal smears and all appeared to have excellent local response. It might be postulated that they all had tumors outside the field of radiation at the time of treatment.

Poor response. The 1 prognostic error (Case P-16) in the poor response group is classified as stage IV and is the only stage IV in the entire group to survive. The 1 smear examined on this patient was taken 4 months after radiation treatment. As stated previously, we know now that it is impractical to judge the response to radiation that long after treatment. It is also somewhat questionable whether this patient was actually a stage IV originally. She had had a combined abdominal perineal resection of an adenocarcinoma of the rectum 3 years previously and therefore no rectal examination was possible. Her pelvis was thought to be entirely fixed at her first examination in the gynecologic tumor clinic. However, it was impossible to say whether this fixation was due to reaction following surgery or to disease.

DISCUSSION

This method of prognosis is based on whether or not the *nonmalignant epithelial cells* react to radiation. Since those patients in whom the epithelial cells showed little change did very poorly, it may be postulated that the tumor shares the resistance of the host to radiation. One may see some evidence of this in the vaginal smear. If the epithelial cells show marked radiation change, the malignant cells also show marked changes. However, if the epithelial cells show little radiation change, the malignant cells show little change. The epithelial cells to a degree mirror the changes in the tumor cells.

One could judge the effect of radiation by examining only the malignant cells for presence or absence of radiation change. However, certain technical difficulties arise. First, the cancer cells present in the vaginal smear are usually in the minority and may be as low as 1 per cent of the total cell population. It is difficult to judge the reaction of cells accurately when few are present. Second, the method depends on well preserved cells being

shed from the surface of a tumor. Often as treatment progresses, the necrotizing effect of radiation will destroy the surface of the tumor so that well preserved cancer cells are not exfoliated. This may be the reason that often in cases in which the epithelial cells show little radiation change, the malignant cells will nevertheless disappear. The presence or absence of malignant cells at the end of treatment is an unreliable prognostic index. Of greater importance in our opinion is whether the malignant cells show indications of having *reacted* to radiation.

It is of interest that by determining the degree of radiation reaction in nonmalignant epithelial cells of the cervix and vagina we can predict quite reliably whether the tumor has responded to radiation. This is especially true in the poor response group in which only 1 patient out of 37 survived. Judging the amount of radiation reaction in the epithelial cells presents none of the difficulties described for malignant cells. The epithelial cells are present in abundance and the radiation changes are so marked they may be easily recognized. One word of caution may be appropriate. This method is not based on *whether* the epithelial cells show radiation change but on *what proportion* of these cells show radiation change. All cases treated by radiation will show some cells exhibiting radiation reaction.

The fact that radiation reaction in normal cells may be used to predict parallel changes in tumor cells is of theoretical significance. It is our impression after studying these 73 cases and an additional hundred cases that there is a spectrum of radiation sensitivity. At one end is the patient who is extremely sensitive to radiation. Case G-10 is an example of this type of sensitivity. She received 7,800 roentgens of x-ray in air. She had a very marked response in the epithelial cells of the vaginal smear. She refused radium treatment. This patient received "inadequate" treatment for her stage II carcinoma yet she is well and without disease at 62 months. At the other end of the spectrum is Case P-3. This patient had a stage II carcinoma clinically and received 6,000 roentgens of x-ray in air and 3,900 milligram hours of radium. The epithelial cells of the vaginal smear showed very little radiation effect. Though she received adequate therapy, her local disease was never controlled and she died 7 months later.

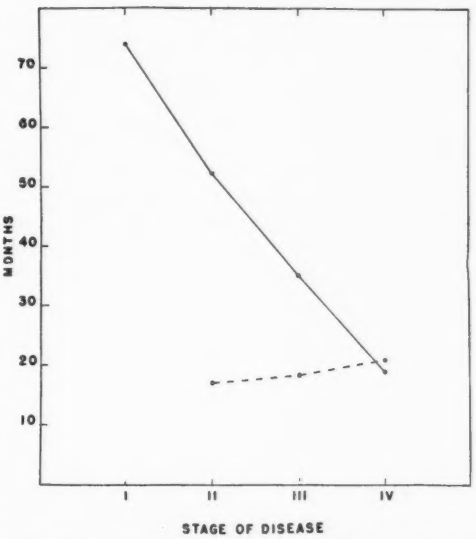

Chart 1. Average survival in months of good and poor response groups. Poor response, - - - - ; good response, ——.

Throughout this series there has never been any correlation between the amount of radiation effect as seen in the vaginal smear and the histologic type of tumor. On the other hand, marked correlation has been found between the clinical extent of disease and the radiation response as judged by the vaginal smear. All the stage I cases showed a good response to radiation, 70 per cent of stage II cases, 30 per cent of stage III cases, and 30 per cent of stage IV cases. As the disease increases in extent, the sensitivity of the individual to radiation, as judged by the epithelial cells, decreases. What factor determines radiation sensitivity is unknown, but here is evidence that it may change. The thought occurs that perhaps it could be changed in the direction of greater sensitivity as well.

The vaginal smear is reliable as a prognostic tool in selecting those patients who do not respond to radiation at the time of their treatment. This should enable the clinician to choose other therapy in the treatment of this group of cervical cancers.

SUMMARY

The 5 year survival of 73 patients with cervical carcinoma treated by irradiation, in which the radiation changes in the benign epithelial cells of the vaginal smear were used as a prognostic index, is reported. The absolute prognostic accuracy in the group was 75 per cent; the relative accuracy 80 per cent. Of the 37 patients judged as poor responses, only 1 has survived 5 years, a prognostic accuracy of 97 per cent. Of the 36 patients judged as good responses, 55 per cent survived 5 years. The amount of radiation change seen in the epithelial cells of the vaginal smear is a reliable prognostic index in cancer of the cervix.

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EDITORIAL

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DECEMBER, 1951

THE ART OF ABDOMINAL PERCUSSION IN THE PRESENCE OF INFLAMMATION

PERCUSSION of the abdomen is a well recognized aid in outlining an enlarged liver or spleen, in determining the presence of free fluid, in delineating the size of an ovarian cyst, an enlarged uterus, or a distended stomach. Its usefulness in the presence of peritoneal inflammation has been generally overlooked. Seek as one may in the large systems of surgery or in special books devoted to physical diagnosis, one finds no mention of this simple maneuver. And yet it can provide most valuable information as to the presence of peritoneal inflammation, its location, and its extent. To me it is the most helpful single diagnostic procedure in evaluating the acutely disturbed abdomen. Long since discarded has been the sign of "rebound tenderness." It is gross, it is cruelly painful, and it is not sufficiently accurate to be helpful when most needed in locating the primary seat of inflammation.

In the appraisal of an abdomen under scrutiny, the patient is not touched until he has been asked to cough. The resulting pain will give the first evidence of the site of inflammation, and of the probable organ or viscus primarily involved. The abdomen is then palpated to determine the presence of muscle guarding. This must be done gently, and painlessly, and is begun in areas away from the site of pain as revealed by coughing. Rarely is guarding absent over areas of inflammation, but it cannot be accurately located by a heavy hand. Gentleness is essential.

Then follows light percussion—also begun in presumably unaffected areas—by working downward from the epigastrium in lower abdominal discomfort, toward the epigastrium in upper abdominal pain, and from the side of comfort to the side of pain in unilateral involvement. The area of tenderness is quickly and easily ascertained, its exact extent is determined and, when deemed important, is outlined on the skin by pencil. All degrees of intensity of tenderness are encountered, shading gradually from the mild tenderness at the periphery to the exquisitely painful percussion at the center of the involved area. The site of greatest tenderness is usually found over the inflammation of longest duration, and this obviously corresponds with the site where the inflammation first began. This may be of real diagnostic importance. For example, a ruptured duodenal ulcer may be accompanied by pain in the right lower quadrant strongly suggesting appendicitis. But if light percussion demonstrates the greatest intensity of tenderness in the right epigastrium, and less tenderness on similar percussion over the right lower quadrant, the diagnosis is ruptured ulcer and

not appendicitis. In lower abdominal peritonitis due to a ruptured diverticulum on the left, bilateral tenderness is usually present, but the most intense discomfort on percussion will be found on the left over the site of inflammation of longest duration, which alone may suggest the proper diagnosis.

In pelvic peritonitis in the female, tenderness on percussion just above the level of the pubes, equally intense on both sides of the midline, suggests inflammation originating in the pelvic organs, whereas tenderness on both sides but greater on the right and growing more intense as McBurney's point is approached suggests that the inflammation began in the appendix. Pain in the right lower quadrant produced by moderate percussion on the *left* side of the abdomen is one of the most conclusive signs that peritoneal inflammation is present on the right at the site of pain, and that the appendix is most probably the culprit. Similarly, pain produced in the upper right quadrant by percussion elsewhere in the abdomen is evidence of peritoneal inflammation having its origin in the gall bladder, in a high-lying appendix or in a penetrating or perforating duodenal ulcer. Gentle percussion to determine the exact site of most intense tenderness will help to identify the offending organ. In a penetrating ulcer it lies high in the epigastrium. In appendicitis the greatest tenderness is located immediately over the site of the inflamed appendix, which may lie high in the upper quadrant but usually lies well below the costal margin. An acutely inflamed gall bladder would be demonstrated by percussion to lie just below the costal margin, and to descend on respiration. In a less acutely inflamed gall bladder, pain on percussion may be absent over the gall bladder area on quiet respiration, but on deep inspiration definite and marked tenderness may be demonstrated to descend below the costal margin. If the necessity for immediate operation is at first debatable, the extent of tenderness is mapped out on the abdominal wall. One or 2 hours later, after the administration of intravenous fluid containing perhaps penicillin or terramycin in appropriate amounts, the abdomen is again subjected to gentle percussion. If the mapped area of tenderness has extended notably, the area of inflammation has increased and operation is indicated. If the mapped area has decreased or is stationary, watchful waiting is in order. Similarly, in a questionable case of appendicitis, decision as to action may be postponed for consideration an hour or so later. At the second examination if percussion tenderness has increased in intensity and extent in the vicinity of McBurney's point, the diagnosis of appendicitis may be made with greater certainty. The area of most acute tenderness on percussion may also be helpful in determining the site of the incision for entering the abdomen, whether through a high or a low lying, muscle splitting incision. If an abscess is present or suspected, the site of greatest tenderness indicates the area nearest the surface and therefore the optimum point for drainage.

Occasionally when localized peritonitis is suspected at the first examination, but not definitely demonstrable, the area of percussion tenderness is carefully demarcated. If at re-examination 1 or 2 hours later, the area of tenderness has increased markedly, the diagnosis of peritonitis becomes more evident. For example, a boy of 10 was said to have been run over by an automobile a few minutes before his admission to the hospital. No telltale marks or signs were present, but there was a small area of exquisite tenderness on percussion halfway between xiphisternum and umbilicus. Rigidity was absent. Two hours later mild muscle guarding had set in and the area of tenderness as determined by percus-

sion had descended well below the umbilicus. The abdomen was promptly opened to find the jejunum torn partially across at the point of fixation to the posterior abdominal wall. Its repair led to an uneventful recovery.

In acute pancreatitis, the tenderness on percussion may outline fairly accurately the anatomical location of the pancreas on both sides of the upper abdomen. It is hoped that this may aid in the more frequent and earlier recognition of the various shades and degrees of a disease hitherto associated with more violent manifestations. Tenderness on percussion in the left upper quadrant over the splenic area may suggest correctly a splenic infarct accompanied by local peritoneal irritation. Its limited and stationary character as determined on repeated examination by percussion rules out the need for operative intervention. In still other circumstances the extent of urinary extravasations may be accurately delineated and may be followed by percussion.

Postoperatively, the progression or regression of peritonitis is followed best by light percussion performed daily in the same manner and under the same circumstances. Palpation is helpful, but not so precise. Moreover, after any intra-abdominal operation, the surgeon can reassure himself daily as to its benign course by the absence of percussion tenderness in areas remote from the operative field. Its subsequent appearance in these areas may be the first harbinger of trouble.

Referred abdominal pain attending the diaphragmatic inflammation of pneumonia may usually be so diagnosed with the demonstration that the peritoneum is not tender on percussion, therefore, not inflamed, and therefore not the primary source of the abdominal pain. A case of abdominal pain unaccompanied by tenderness anywhere on moderate to heavy percussion may be confidently held for further observation without fear that an acute surgical emergency is being overlooked.

Other situations and circumstances will afford the interested surgeon many opportunities to appraise the value of percussion in determining more accurately the character, the degree and the extent of inflammation and irritation within the abdomen. Students generally and house officers in particular should seek to perfect themselves in the art of abdominal percussion. EMILE HOLMAN.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THOSE members of the profession who can read German will find the *Spezielle Pathologie der Krankheiten des zentralen und peripheren Nervensystems*[1] an excellent book. The author, who is Professor of Neurology and Psychiatry at the University of Bonn, has covered the field of neuropathology systematically and thoroughly and he has done this within a reasonable number of pages. It is a book in the tradition of Spielmeyer and Buechner and is modern in its approach. The illustrations set a high standard of excellence and the typography and craftsmanship of the book are wholly pleasing. This is the second German textbook, which I have recently read, that surpasses comparable American books in the excellence of reproduction of illustrations and of general format. Should this not be a challenge to our publishers? WILLIAM B. WARTMAN.

ACCORDING to the author, the volume *Syllabus of Human Neoplasms*[2] has been organized with the thought of presenting the basic fundamentals of malignant disease in man.

There is a brief summation of the problem of cancer followed by chapters on epithelial neoplasms of skin and appendages, neoplasms of mesenchymal origin, of neuroectodermal origin, of the alimentary tract, of the respiratory tract, of the urinary tract, of male genitalia, of female genitalia, and of endocrine glands. There is a section of miscellaneous neoplasms and last, a supplement containing descriptions of less common and more recently discussed new growths. Black and white photomicrographs are well selected and illustrate the more common as well as some of the rare entities. A bibliography is included at the end of each chapter.

Although basically pathologic, there is sufficient clinical and statistical data to maintain a stimulating delineation of the subject for those who are not primarily concerned in pathology.

This reviewer wonders why there are paragraphs on Addison's disease, Simmonds' disease, cervicitis, and other lesions not considered neoplastic. Their method of presentation is satisfactory but space would have been saved for lengthier discussion of some tumors.

The style of writing is clear, the sentences are short and informative, and the number of paragraphs alloted each entity is in proportion to its importance. Controversial comments are avoided. For those who require much information on cancer in man in a short reading time, this volume may be readily recommended. M. C. WHEELOCK.

THE short volume of 147 pages *Lumbar Puncture and Spinal Analgesia*[3] contains some extremely useful information on lumbar puncture and spinal analgesia, beginning with a brief history and ending with "do's, don'ts, and doubtfuls." Much of the book is taken up with very excellent drawings and illustrations. Technique and positions are described and illustrated. The chapters on anatomy and cerebrospinal fluid are simple and lucid. Complications other than headache are discussed briefly or not at all. Spinal drugs and dosages are mentioned only in passing. The bibliography is extensive and the index is excellent. The book is readable and is recommended for the student in anesthesia and others who wish to become conversant with good spinal technique. LUCILLE WATT.

THE book *The Human Colon; an Experimental Study Based on Direct Observation of Four Fistulous Subjects*[4] is a fascinating and learned documentation of the effects of pharmacologic, physical, and psychic stimuli on the colon. The authors have used the direct approach to record a detailed and comprehensive series of observations of subjects with large segments of colon evaginated and permanently exposed on the abdominal wall. In two subjects the fistula exposed the right colon, in another the middle or transverse colon, and in the fourth the left colon.

This report concerns itself chiefly with those phenomena in day to day experience that modify colonic function, i.e., anger, fear, contentment, depression, pain, happiness, and so forth. The results are illustrated in striking full color photographs and easily interpreted schematic charts and graphs. Secretory and circulatory changes, lysozym concentration, motor activity, and mucosal fragility were investigated in each patient. When these factors were studied in connection with ulcerative colitis before and after vagotomy, no evidence was forthcoming that such a procedure altered the be-

[1] SPEZIELLE PATHOLOGIE DER KRANKHEITEN DES ZENTRALEN UND PERIPHEREN NERVENSYSTEMS. By Dr. Gerd Peters. Stuttgart: Georg Thieme, 1951.

[2] SYLLABUS OF HUMAN NEOPLASMS. By R. M. Mulligan, M.D. Philadelphia: Lea & Febiger, 1951.

[3] LUMBAR PUNCTURE AND SPINAL ANALGESIA. By R. R. Macintosh, M.A., D.M., F.R.C.S. (Edin.), D.A. Baltimore: The Williams & Wilkins Co., 1951.

[4] THE HUMAN COLON; AN EXPERIMENTAL STUDY BASED ON DIRECT OBSERVATION OF FOUR FISTULOUS SUBJECTS. By William J. Grace, M.D., Stewart Wolf, M.D., and Harold G. Wolff, M.D. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1951.

havior of the colon or protected it from acute exacerbations.

The authors conclude that the colon of man is likely to participate in his reaction patterns to threatening events and that changes involving colonic hyperfunction, at first altogether functional and transitory, may, when unduly sustained, result in structural damage and disease. One is impressed by the fact that this volume could only have been produced as the result of long, arduous, and painstaking observation. To those interested in colon disease, whether it be medical or surgical, or in any phase of psychosomatic medicine this book will prove to be of interest and value. THOMAS J. MERAR.

THE volume entitled *A History of Neurological Surgery*[1] is the first attempt of its kind to cover the entire history of neurological surgery, going far back into the pre-Christian eras of medicine and surgery. Actually the book is more than a history of neurological surgery, since the foundations of neurosurgery obviously had their beginnings in neurology, general surgery, and general medicine, and many of the founders of the art as it is practiced today were men of general surgical interest or teachers with a fundamental interest in physiology. The students of Johns Hopkins University are indeed fortunate to have had presented to them in medical lectures the essays of which this monograph is the result. The book is a wealth of material which in truth is the essence of that type of information so necessary to the well rounded student and so frequently lacking in this day of compressed and harassed curricula in medical schools.

There is a quiet vein of humor present in many of the chapters, exemplified, for instance, by the unembellished statements of beliefs and practices of various neurosurgeons (without any comment, agreement, or disagreement on the part of the essayist) concerning those matters which have come to be well established controversies and bones of contention among certain neurosurgeons still living.

The book is interspersed with quotations from publications, ancient and modern, as for instance those on pages 111, 321, 425, and various others so that there is no chance that the reader will become bored by what he might feel to be a dull historical account. There are brief and quite well written biographical sketches scattered through the book of the following well known persons: Cushing, Dandy, Vincent, Horsley, Macewen, von Bergmann, Krause, Puusepp, Foerster, Frazier, Balado, Elsberg, de Martel and Peet.

The text comprises 458 pages. In the bibliography of 102 pages there is the amazing number of 2,371 references. The volume is well indexed in 21 pages and the printing and illustrations are of first quality. The book certainly is recommended to all lovers of medical and surgical history, to all students of neurology and neurosurgery, and it will, no doubt, be used extensively as a source book because of the unusual bibliography. JOHN MARTIN.

[1]A HISTORY OF NEUROLOGICAL SURGERY. Edited by A. Earl Walker, M.D. Baltimore: The Williams & Wilkins Co., 1951.

THE new work *Tumors of the Eye*[2] by Reese fills a long felt need for a monograph on tumors of the eye, and he has done a marvellous and monumental job of collecting the information of the past half century pertaining to this subject.

The book is divided into 7 chapters, each of which deals with one of the seventeen different types of tumors of the eye and its adnexa. The space devoted to each is proportionate to relative importance and frequency.

The author deals exhaustively with the diagnosis, differential diagnosis, histopathology, prognosis, and treatment of the common neoplasms, and includes many original observations. The chapters on retinoblastoma, glioma, pigmented tumors, and angiomatous tumors are outstanding examples of the successful integration of original thought and results of personal research with the traditional viewpoint of various phases in the diagnosis and management of ocular neoplasms. The rare tumors are discussed sufficiently for practical purposes and the book is complete in its scope.

Whenever possible the author draws upon his own rich experiences, which gives many chapters the refreshing spontaneity of an eye witness account. At the same time the contributions of other investigators to the subject are duly credited and there is a comprehensive, up-to-date bibliography of the significant literature at the end of each chapter.

The illustrations are beautiful and placed in the text so as to be easily accessible. The outstanding character of the reproductions of the illustrations and the generally superlative quality of the format of the book represent an additional triumph in the series of ophthalmic monographs produced in recent years by Paul B. Hoeber.

This is an interesting and exceedingly practical volume, not only for the ophthalmologist but for any other medical specialist who may encounter tumors of the eye and its adnexa and their often far-reaching complications and surprising associations with remote organs of the body.

BERTHA A. KLIEN.

THE new textbook, in German, of practical and topographical anatomy by Professor Töndury,[3] of Zurich, is a volume prepared for both students and practitioners.

The ample sections deal, in familiar succession, with the thorax, abdomen, pelvis and perineum, back, head, neck, upper extremity, and lower extremity. Typically, each section begins with a discussion of the embryology of the part, continues to a consideration of the applied gross anatomy—in-

[2]TUMORS OF THE EYE. By Algernon B. Reese, M.D., D.Sc. (Hon.), F.A.C.S. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1951.

[3]ANGEWANDTE UND TOPOGRAPHISCHE ANATOMIE; EIN LEHRBUCH FUER STUDIERENDE UND AERZTE. By Prof. Dr. G. Töndury. Stuttgart: Georg Thieme, 1951.

cluding striking variations, and the radiographic appearance of skeleton and tubular organs.

The excellent illustrations fall into two main categories, those dealing with the standard treatment of muscles, viscera, nerves, and vessels, and those depicting variations and topographical relationships. The figures in the former category appear as individual, page-sized halftones, many of them in full color; those of the latter type are plain zinc, distributed through the text.

The concise text is highly instructive and basically dynamic; the book is of convenient size. In all respects the *Anatomie* is a credit to the high tradition of continental scholarship. BARRY ANSON.

THE excellent *A Textbook of Medicine*[1] for the medical student and the practicing physician has just been completely revised. Doctor Cecil, assisted by Dr. Robert E. Loeb in this new (8th) edition, with their distinguished coeditors and contributors—168 in all—have virtually rewritten the entire book to bring all of the best authoritative opinion on diagnosis and treatment to the medical profession. This edition maintains its time tested characteristics of completeness, authority, and balanced presentation.

This textbook has always emphasized symptoms and in this latest edition the authors have added a great deal of fresh, new information on the underlying pathologic physiology and biochemistry, which give rise to jaundice, shortness of breath, edema, cyanosis, pallor, weight loss, pain, and many other deviations from the normal. This information is distributed throughout the book in conjunction with the various diseases being described.

The complete story of any disease is located in one place in this textbook. Etiology, signs and symptoms with the underlying pathology, diagnosis and differential diagnosis, prognosis, and treatment are all discussed crisply and thoroughly in the light of the latest acceptable knowledge. Great emphasis is laid on the proper integration of pertinent, basic medical information, such as biochemistry, normal and pathologic physiology, and a good amount of psychology with the description of each disease.

The psychosomatic aspect of medicine has been duly stressed. There is an excellent separate section on the main psychiatric deviations, but also throughout the book, psychotherapy is pointed up whether it be with the obviously ill patient with cardiac or hyperthyroid disease or the troubled individual who may or may not harbor organic disease.

The new (8th) edition has been expanded to include 20 new subjects yet the book has been made slim (it is actually 136 pages smaller than previous editions) because of careful editorial work which allots to each disease only as much space as its importance warrants. Repetition is avoided by including only once the basic material already mentioned. As an example—the infectious diseases, which have been brought under control so dramatically by the "newer drugs," are given less space in this edition.

Fundamental information is well handled, such as the discussion of heart failure which begins on page 1051, with a very full account of the physiological factors and changes which lead to circulatory failure. Both backward and forward failure are described giving the pathogenesis of symptoms which are traceable to each; then discussions are given of dyspnea, cyanosis, edema, and so forth. This all inclusive discussion requires little more than 11 pages.

Again in kidney disease, which begins on page 908, the normal physiology of the kidney is discussed, the renal function tests are given, and then basic deviations from the normal (undersecretion and oversecretion) physiology are discussed. Finally, this is followed by specific disease entities such as nephritis.

Throughout the book where each disease is discussed, the complete story is given for that particular disease from the earliest signs and symptoms to the final diagnoses and treatment. Pertinent references in the literature are given at the end of each discussion.

A table listing the "Normal Laboratory Values of Clinical Importance" and a splendid cross index occupy the last 176 pages of this textbook.

Every chapter in Cecil and Loeb is marked by basic biochemical and physiological information which makes it an excellent textbook for the student beginning the study of internal medicine and the completeness of the discussion with excellent references should make it also invaluable to the practitioner of medicine. GEORGE C. TURNBULL.

THE author of *Scoliosis; Pathology, Etiology, and Treatment*,[2] Dr. Kleinberg is an eminent orthopedic surgeon who, during his long career has had a special interest in the understanding and treatment of scoliosis. This monograph on scoliosis is based on his long experience with this very difficult orthopedic condition.

The author aims to present the modern concept of the pathogenesis of scoliosis and to elaborate on the knowledge of etiology and at the same time review the results of conservative and surgical measures in the treatment.

He attempts to classify the types so that the prognosis and the most favorable program of therapy can be prescribed. The author believes that the knowledge of etiology has been increased and that there is some hope in such procedures as alteration of the epiphyseal growth. He also believes that heredity plays a role and that nearly 25 per cent of the cases are inherited. He emphasizes that the treatment is time-consuming and may take 5 to 10 years.

[1] A TEXTBOOK OF MEDICINE. Edited by Russell L. Cecil, Robert F. Loeb, M.D., assisted by Alexander B. Gutman, Walsh McDermott, M.D., and Harold G. Wolff, M.D. 8th ed. Philadelphia and London: W. B. Saunders Co., 1951.

[2] SCOLIOSIS; PATHOLOGY, ETIOLOGY, AND TREATMENT. By Samuel Kleinberg, M.D. Baltimore: The Williams & Wilkins Co., 1951.

The subject matter includes a thorough discourse on the anatomy, embryology, and physiology as well as the pathology. There is a long discourse on etiology with such classifications as functional scoliosis and idiopathic scoliosis still included. He discusses prophylaxis of scoliosis, particularly with regard to the types of known origin. He distinguishes still between a functional scoliosis and a structural scoliosis and classifies the treatment accordingly.

The techniques on treatment are well described but treatment still leaves a great deal to be sought for.

The format is good, with excellent paper and type. There are many excellent illustrations.

EMIL D. W. HAUSER.

THE book *Cystectomy for Cancer of the Urinary Bladder*[1] by Boeminghaus is a short monograph of 84 pages which was written mainly to stimulate a renewed interest in cystectomy among German urologists. Since his own experience with this procedure is limited to 14 cases, the author has drawn heavily upon the publications of others, especially those of Millin and Couvelaire. The treatment of carcinoma of the urinary bladder is reviewed objectively and the subject is presented with a mature skepticism born of the author's long and varied experience.

The indications for and the technique of cystectomy are presented in detail. In spite of its brevity this monograph is remarkably complete and well written. The illustrations are excellent.

FREDERICK A. LLOYD.

THE 10th edition of *Principles and Practice of Obstetrics*[2] has been thoroughly revised and rewritten. Clinically unimportant discussions, such as the rare spontaneous delivery of a transverse presentation, to which in the older editions so much space was devoted have been drastically cut. Prominent specialists outside the field of obstetrics have been called upon to edit and to write certain portions of the book (erythroblastosis, psychology of women, anesthesia and heart disease), thus introducing a broader outlook than the obstetrician alone can offer.

In most instances specific recommendations for treatment are outlined and this combined with a complete discussion of diagnosis and pathology make the volume a more practical reference than recent editions have been. The bibliography is moderately extensive and up-to-date and includes many foreign references. In general, this is a book which should be equally valuable to the medical student and the doctor in practice since it includes both fundamental basic information necessary to understand obstetric conditions and specific recommendations for the management of problems.

J. ROBERT WILLSON.

[1] CYSTEKTOMIE BEIM BLASENKREBS. By Prof. Dr. H. Boeminghaus. Düsseldorf, Stuttgart: Georg Thieme, 1951.

[2] PRINCIPLES AND PRACTICE OF OBSTETRICS. By J. P. Greenhill, M.D. 10th ed. Philadelphia, W. B. Saunders Co., 1951.

THE book entitled *Anatomy in Surgery*[3] by Philip Thorek is primarily a text on anatomy into which a section on surgical considerations has been inserted giving some of the more commonly performed operative procedures in anatomical detail. The volume is 916 pages in length, has a table of contents, and a good index appended.

One of the best features of the book is the 720 illustrations drawn by one artist, which though somewhat diagrammatic, are excellently drawn and well placed to illustrate the text. Many of these are in color. The legends and labels are well done and of such size that they are easily read.

The book is divided into ten sections each representing a region of the body. For convenience the various subheads of these sections are described under numbered subsections. The text is written in an informal style which makes it easy to read. This good quality of the text is somewhat enhanced by the elimination of tedious anatomical detail found in most anatomical texts.

This book may enlighten the medical student on the surgical importance of a region while studying anatomy for the first time and later he may review it to refresh his knowledge of anatomy while studying surgery. The brevity of the sections on surgical considerations and the failure to present a choice of surgical procedures makes the volume somewhat less useful for the surgeon.

THOMAS C. DOUGLASS.

THE third edition of Grant's *An Atlas of Anatomy*[4] is now in one volume. In the new edition additional illustrations have been incorporated and some of the former illustrations have been replaced or improved. The author, his collaborators, and the artist are to be commended, for the most part, in selecting suitable dissections which depict the anatomical structures throughout the body with accuracy. The illustrations and the labeling of the various structures are of sufficient size to lend themselves to easy identification.

The illustrations of the female perineum are not up to standard with the rest of the atlas. As presented in the atlas the first year student in anatomy may encounter some difficulty in interpreting the relationships of the neurovascular structures and the perineal musculature to the various fascial layers. More dissections illustrating the fascial planes and the various components of the urogenital and pelvic diaphragm would appear to be in order.

Of special interest to the student of anatomy will be the information concerning the variations and anomalies, with their frequency of occurrence, of many anatomical structures; the presentation of the bronchopulmonary segments with illustrations of their surface topography; and the scheme of distribution of the cranial nerves and the dermatomes of the body.

[3] ANATOMY IN SURGERY. By Philip Thorek, M.D., F.A.C.S., F.I.C.S. Philadelphia, London, Montreal: J. B. Lippincott Co., 1951.

[4] AN ATLAS OF ANATOMY. By J. C. Boileau Grant. 3d ed. Baltimore: The Williams & Wilkins Co., 1951.

The medical student, surgical resident, or surgeon who wishes an atlas of anatomy for dissecting purposes or for review will not err in selecting this book.

LA VERN SWIGART.

THE interesting volume *Meister der Chirurgie und die Chirurgenschulen im deutschen Raum*[1] begins with a historical chapter which comprises a very excellent review of the development of surgery from the middle of the nineteenth century. Accompanying it are the likenesses of 32 men, beginning with Albertus Magnus and Paré and ending with von Volkmann and Kocher, whose contributions to the development of surgery are particularly stressed.

In succeeding pages the universities of the German realm, beginning with the University of Prague, are listed in the chronological order of their foundation. A chapter is devoted to each of 35 universities, beginning with those of Prague, Vienna, Heidelberg, Cologne, Wurzburg, and Leipzig, and in each chapter paragraphs of varying length are devoted to the academic record and contributions of the successive professors of surgery in each institution during the past two hundred years.

A mass of interesting data and information is compressed in these paragraphs with the result that the volume becomes practically an encyclopedia of the careers and achievements of the German speaking surgeons of the past two centuries.

SUMNER L. KOCH.

A comparatively new field is covered in an excellent manner in Campbell's *Clinical Pediatric Urology*.[2] This field has developed rapidly since the introduction of excretory urography, and additional advances have been aided by the development of miniature cystoscopes and other urologic instruments.

Every phase of pediatric urology is covered in one volume. The work has been carefully planned. The general arrangement is simple and straightforward. The binding, typography, and paper are pleasing, and the illustrations are a credit to both author and publisher.

The allocation of space in the discussion of the various topics has been governed by the incidence and relative importance of the conditions. The author has cited the work of others very freely, and the extensive bibliography has been gathered from the world's literature. Fortunately, the whole presentation reflects much clinical data from the author's wide experience.

This book will appeal to most of the profession.

D. O. FERRIS.

[1]MEISTER DER CHIRURGIE UND DIE CHIRURGENSCHULEN IM DEUTSCHEN RAUM. By Prof. Dr. H. Killian and G. Kraemer. Stuttgart: Georg Thieme, 1951.

[2]CLINICAL PEDIATRIC UROLOGY. By Meredith Campbell, M.S., M.D., F.A.C.S. Philadelphia: W. B. Saunders Co., 1951.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ROENTGEN ANATOMY; ROENTGEN ANATOMÍA. By David Steel, M.D. Springfield, Ill.: Charles C Thomas, 1951.

THE HEALING TOUCH. By Harley Williams. Springfield, Ill.: Charles C Thomas, 1951.

HORMONES AND BODY WATER. By Robert Gaunt, Ph.D., and James H. Birnie, Ph.D. Springfield, Ill.: Charles C Thomas, 1951.

RENAL PELVIS AND URETER. By Peter A. Narath, M.D., F.I.C.S. New York: Grune & Stratton, 1951.

SURGICAL CARE; A PRACTICAL PHYSIOLOGIC GUIDE. By Robert Elman, M.D., F.A.C.S. New York: Appleton-Century-Crofts, Inc., 1951.

711 MEDICAL MAXIMS. By William S. Reveno, M.D. Springfield, Ill.: Charles C Thomas, 1951.

LECCIONES DE FISIOPATOLOGIA Y CLINICA QUIRURGICA. By Prof. Francisco Martin Lagos. Vol. 1, 2d ed. Barcelona, Madrid, Lisboa, Valencia: Editorial Cientifico Medica, 1950.

PEPTIC ULCER; CLINICAL ASPECTS; DIAGNOSIS; MANAGEMENT. Edited by David J. Sandweiss, M.D., F.A.C.P. Philadelphia, London: W. B. Saunders Co., 1951.

THE CHILD UNBORN. By R. J. Harrison, M.A., S.Sc., M.B., B.Chir., F.I.S. New York: The Macmillan Co., 1951.

MEDICAL TERMINOLOGY MADE EASY. By JeHarned, R.N., R.R.L. Chicago: Physicians' Record Co., 1951.

CONGENITAL DISLOCATION OF THE HIP. By Julius Hass, M.D. Springfield, Ill.: Charles C Thomas, 1951.

GYNAECOLOGICAL ENDOCRINOLOGY FOR THE PRACTITIONER. By P. M. F. Bishop, D.M. (Oxon.). 2d ed. Baltimore: The Williams & Wilkins Co., 1951.

EXERCISES AFTER CHILDBIRTH. By Gertrude Behn, M.C.P.S., with a foreword by Linton Snaith, M.D., Edinburgh: E. & S. Livingstone Ltd., 1951.

APPROVED LABORATORY TECHNIC. By John A. Kolmer, M.D., D.P.H., Sc.D., F.A.C.P., Earle H. Spaulding, Ph.D., and Howard W. Robinson, Ph.D. 5th ed. New York: Appleton-Century-Crofts, Inc., 1951.

SURGICAL MEASURES IN HYPERTENSION. By Reginald H. Smithwick, M.D. Springfield, Ill.: Charles C Thomas, 1951.

ANGIOCARDIOGRAPHY. By Charles T. Dotter, M.D., and Israel Steinberg, M.D. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1951.

AUTOPSY DIAGNOSIS AND TECHNIC. By Otto Saphir, M.D. 3d rev. enl. ed. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1951.

AN ATLAS OF NORMAL RADIOGRAPHIC ANATOMY. By Isadore Meschan, M.A., M.D. Philadelphia, London: W. B. Saunders Co., 1951.

PSYCHOSOMATIC GYNECOLOGY: INCLUDING PROBLEMS OF OBSTETRICAL CARE. By William S. Kroger, M.D., and S. Charles Freed, M.D. Philadelphia, London: W. B. Saunders Co., 1951.

FRONTAL LOBOTOMY AND AFFECTIVE BEHAVIOR; A NEUROPHYSIOLOGICAL ANALYSIS. By John F. Fulton, M.D. New York: W. W. Norton & Co., 1951.

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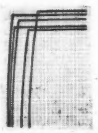

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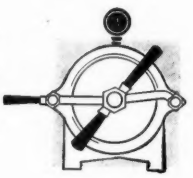

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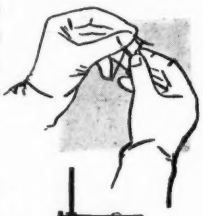

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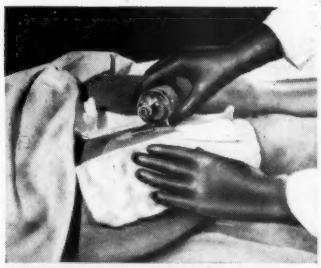

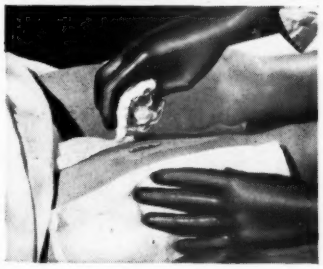

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